Breast Cancer in Ontario
1971-1996

Preface/Highlights/Background

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Preface

This monograph presents information on incidence, mortality and survival for invasive breast cancer in Ontario females from 1971 to 1996. It was developed to provide comprehensive background information for the Ontario Breast Screening Program (OBSP) and as a resource document for planning.

The basis for the information in this monograph is the Ontario Cancer Registry (OCR). Both the OBSP and the OCR are operated by Cancer Care Ontario (CCO), through funding by the Ontario Ministry of Health and Long-Term Care. The OBSP and the OCR are situated within the Screening Unit and the Surveillance Unit, respectively, of the Division of Preventive Oncology, which is located at the Provincial Office of CCO in Toronto.

The authors would like to thank Drs. Frances O'Malley and Carol Sawka for contributing to the clinical sections in the background and to Mr. Gordon Fehringer for providing projected numbers for breast cancer cases and deaths. We are also grateful to Dr. Richard Schabas, Head of the Division of Preventive Oncology and Dr. Verna Mai, Director of the Screening Unit, for reviewing a draft of this document.

This monograph could not have been produced without the valuable assistance of Mrs. Virginia Hunter (desktop publishing), and Ms. Vicky Majpruz-Moat and Ms. Sandrene Chin Cheong (technical support and graphics). Finally, the authors would like to acknowledge the contribution of all the operations staff within the Surveillance Unit, and the Registry Support Group (within the Information Systems Department), for their ongoing efforts in ensuring the generation of timely and high-quality cancer incidence data for Ontario.

Report Highlights

- In the year 2000, breast cancer will be diagnosed in an estimated 7,200 Ontario women and an estimated 2,000 women will die from the disease.

- In 1992-1996, breast cancer was the most common cancer site among women, representing 29% of the total cancers, and ranked first for every age group. Breast cancer was also the most common cause of death during this time period, accounting for 19% of all cancer deaths.

- Breast cancer incidence varies dramatically around the world. Ontario's incidence rate is among the highest in the world.

- The incidence of breast cancer in Ontario has increased by 17% from 1971 to 1996. This increase was highest for women over 50 years of age, particularly after 1986.

- Mortality rates increased slightly (4%) from 1971 to 1986. Between 1986 and 1996, breast cancer mortality decreased by 9%. This decline was greatest for women aged 40-49 and 50-69. The decline is most likely due both to screening and improved treatments.

- The five-year relative survival rate after diagnosis of breast cancer is 81%. The greatest improvements in survival occurred during the 1980s. Relative survival was highest for women diagnosed at ages 40-69 and lowest for women diagnosed at ages 20-39.

Background

Introduction

About 7,200 Ontario women will be diagnosed with breast cancer in 2000 and an estimated 2,000 women will die from it. Breast cancer is the most common cancer in Ontario women. Although lung cancer causes more deaths overall, breast cancer is the most common fatal cancer in women under age 50. Incidence and mortality are higher, however, for older age groups; the probability of developing breast cancer increases steeply as a woman ages (Table 1). The overall incidence rate increased by 17% between 1971 and 1996. In contrast, the mortality rate increased slightly (4%) from 1971 to 1986 and has been declining since this time.

Table 1. Probability[1] of developing breast cancer by age, and lifetime probability of dying from breast cancer, in Canada (NCIC 2000)

Cumulative probability[1] (%) of developing breast cancer by age:							Lifetime probability of dying	
Age	40	50	60	70	80	90	%	One in:
Probability	0.4	1.7	4.0	6.9	10.1	12.3	3.9	25.8

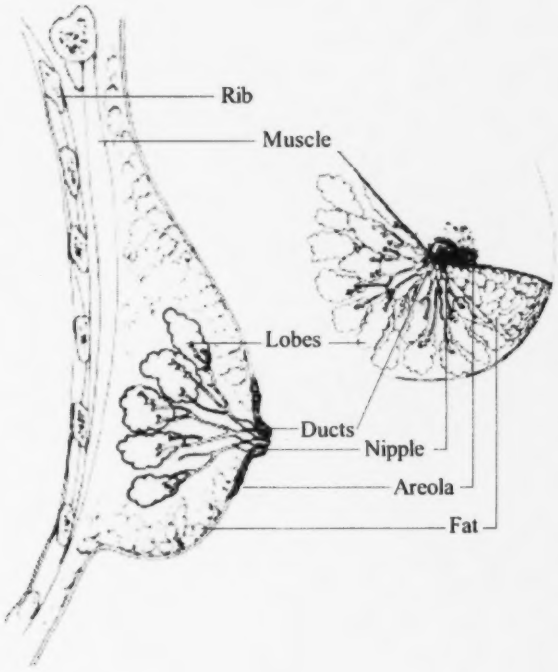
[1] The probability of developing cancer is calculated based on age- and sex-specific cancer incidence and mortality rates for Canada in 1995 and on life tables based on 1994-1996 all-cause mortality rates. The probability of dying from cancer represents the proportion of persons dying from cancer in a cohort subjected to the mortality conditions prevailing in the population at large in 1997.

This report only examines invasive breast cancer in women. Men also get breast cancer. Male breast cancer is not included in this report because there are only about 40 cases diagnosed in Ontario in any year. Such small numbers make it difficult to make meaningful observations about time trends and geographic patterns.

Anatomy

The female breast consists of three major components: glandular tissue, subcutaneous tissue and skin. The glandular tissue consists of breast parenchyma and stroma. The tip of the nipple contains openings of collecting ducts through which the infant obtains milk. The ducts extend from the nipple to form a branching duct system that divides the breast into approximately 20 lobes (Figure 1). Each duct drains a lobe and each lobe comprises 20-40 lobules. Lobules are formed by multiple blind ending branches of the terminal ducts.

Figure 1. Anatomy of the female breast



Source: National Cancer Institute

Pathology of invasive carcinoma of the breast

Invasive carcinoma of the breast is usually divided into tumours of no special morphologic type (infiltrating duct) and those of a special type. Infiltrating duct carcinoma comprises approximately 70% of breast cancers (Berg and Hutter 1995). These tumours can be stratified into prognostic groups based on histologic grading.

Other types of carcinoma comprise approximately 30% of all invasive breast cancers (Page *et al.* 1987). These include lobular, mucinous, tubular, cribriform and medullary cancers. Tubular and cribriform cancers are generally associated with a more favourable prognosis than the other types.

Risk factors

Age is the most significant risk factor for breast cancer. The risk of a woman developing breast cancer increases rapidly with age (Bryant and Brasher 1994). Being born in North America or Northern Europe is also an important risk factor for breast cancer. Risk is slightly higher for women living in urban areas and belonging to a higher socioeconomic class (Kelsey and Bernstein 1996).

Some reproductive characteristics influence the risk of breast cancer. Early age at menarche, late age at menopause, late age at first full-term pregnancy and never having had children are all associated with modest elevations in risk (Kelsey *et al.* 1993). Removal of ovaries before age 40 reduces the risk by about one-half. Women currently using oral contraceptives (OC) are at a slightly increased risk of developing breast cancer, but there is no increased risk 10 years after stopping OC use (Collaborative Group on Hormonal Factors in Breast Cancer 1996). Hormone replacement therapy slightly increases risk and this risk increases with length of use (Collaborative Group on Hormonal Factors in Breast Cancer 1997). This excess risk decreases after hormone replacement therapy is stopped and has largely disappeared after five years. Recent data show that replacement therapy with both estrogen and progestin increases breast cancer risk beyond that associated with replacement with estrogen alone (Schairer *et al.* 2000).

A family history of breast cancer is an important risk factor (Pharoah *et al.* 1997). This risk is particularly high if both the mother and a sister have been affected at a younger age (less than 50). Mutations in several identified genes account for some of this familial clustering. Mutations in the BRCA1 and BCRA2 genes are associated with an inherited susceptibility to breast cancer at an early age and are estimated to account for between 3% and 8% of all breast cancers (Brody and Biesecker 1998).

Many studies have suggested causal roles for diet and alcohol consumption in breast cancer; these remain unverified (Clavel-Chapelon *et al.* 1997; Longnecker 1994).

Postmenopausal obesity increases the risk of breast cancer. Obesity before the menopause, however, is protective (Hunter and Willett 1993; Ursin *et al.* 1995). Regular physical exercise probably reduces the risk of breast cancer, in particular for premenopausal women who are lean and have been pregnant (Friedenreich *et al.* 1998).

Moderate to high doses of ionizing radiation to the chest before age 40 increases breast cancer risk. Results from studies of other exogenous exposures are inconclusive. The most recent large studies have found no evidence of an increased breast cancer risk associated with exposure to environmental pollutants such as the pesticide DDE (chemically related to DDT) and PCBs (polychlorinated biphenyls) (Laden and Hunter 1998).

A number of breast conditions are considered predisposing or predictive factors. Benign proliferative breast disease with atypical hyperplasia increases the risk of breast cancer three- to five-fold and relative risks of around 2 have been found for proliferative disease without atypia (Kelsey and Bernstein 1996). Women with ductal carcinoma in situ, lobular carcinoma in situ, or a history of cancer in one breast are at high risk. Women with high (>75%) mammographic density (the proportion of connective tissue and epithelial tissue as opposed to fat) have a risk three to four times that of women whose parenchyma is mostly fat (Oza and Boyd 1993).

Prevention and early detection

Most of the established risk factors for breast cancer are associated with only moderate elevations in risk. Only a few are readily modifiable by either environmental or behavioural changes. Despite this, some primary prevention trials are underway or planned. Two randomized trials being conducted in North America will assess whether a low-fat diet reduces the incidence of breast cancer (Self *et al.* 1988; Boyd *et al.* 1997). A small randomized trial in Los Angeles, California, is testing whether a hormonal contraceptive regimen designed to suppress ovarian function lowers breast cancer risk (Spicer *et al.* 1993).

Tamoxifen is being considered for the prevention of breast cancer because of its demonstrated effect in decreasing the risk of breast cancer recurrence. Results of three randomized controlled trials have recently been published. Preliminary results of the National Surgical Adjuvant Breast and Bowel Project (P-1) in the United States and Canada showed that tamoxifen use lowers the risk of breast cancer by 45% among users compared to women with the same risk factors who did not take tamoxifen (Fisher *et al.* 1998). Neither the British nor Italian trials have found any benefit from tamoxifen (Powles *et al.* 1998; Veronesi *et al.* 1998).

Screening with regular mammograms can reduce breast cancer mortality in women aged 50-74. Randomized controlled trials show a mortality reduction of 26% (95% confidence interval 17% to 34%) (Kerlikowske *et al.* 1995).

An organized breast cancer screening program was introduced in Ontario in 1990. The Ontario Breast Screening Program (OBSP) offers biennial screening to all women in the province 50 years of age and older. The OBSP offers eligible women two-view mammography, clinical breast examination by a specially trained nurse examiner, instruction in breast self-examination and client recall.

In 1996-97, 61.5% of women aged 50-69 reported having had a screening mammogram in the last two years (Table 2). Only 11.6% of all Ontario women in that age group were screened within the OBSP. OBSP coverage was higher for some regions in the north such as Manitoulin Island and Sudbury and Thunder Bay, Kenora and Rainy River. Expansion of the OBSP since 1998 has increased the proportion of women 50-69 having their screening mammograms within the OBSP to 15.8% during 1998-1999. In 2000, OBSP will reach an estimated 21% of eligible women.

Table 2. Proportion of Ontario women aged 50-69 having a screening mammogram within the last two years, reported by the NPHS and within the OBSP, by region, 1996-1997

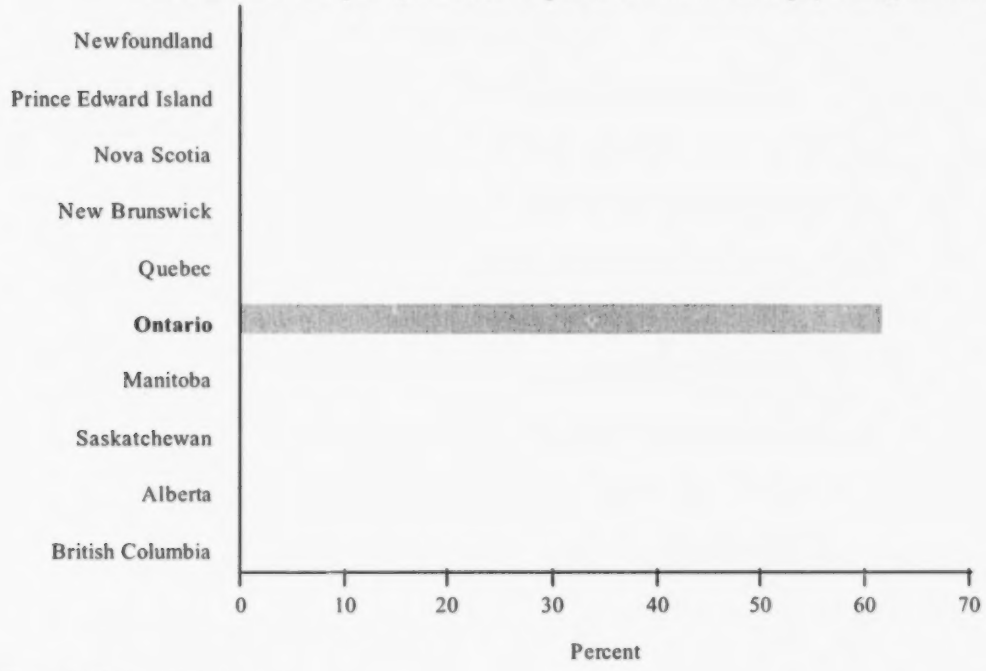
National Population Health Survey (NPHS) Region[1]	NPHS (%)	OBSP[2] (%)
Algoma, Cochrane	63.7	24.5
Brant, Haldimand-Norfolk	50.3	3.4
Bruce, Grey, Perth, Huron	58.2	12.1
Durham	63.8	2.9
Elgin, Middlesex, Oxford	57.4	20.4
Essex	65.2	17.6
Halton	57.4	3.6
Hamilton-Wentworth	61.1	27.4
Lambton, Kent	73.3	6.2
Lanark, Leeds & Grenville, Hastings, Prince Edward, Frontenac, Lennox & Addington	58.2	24.3
Manitoulin Island, Sudbury District, Sudbury Regional Municipality	66.3	43.1
Niagara	61.4	1.6
Northumberland, Victoria, Haliburton, Peterborough	67.3	6.7
Ottawa-Carleton	62.3	22.7
Peel	58.6	0.8
Prescott & Russell, Stormont-Dundas & Glengarry, Renfrew	59.3	10.8
Simcoe	58.3	1.5
Thunder Bay, Kenora, Rainy River	65.1	30.0
Timiskaming, Muskoka, Parry Sound, Nipissing	48.9	8.0
Toronto	63.7	7.8
Waterloo	56.1	6.6
Wellington, Dufferin	64.2	7.3
York	67.0	6.7
All Ontario	**61.5**	**11.6**

[1] Regions are agglomerations of census divisions

[2] Number of women aged 50-69 at screening who participated in OBSP as a proportion of all women aged 50-69 in that region, using 1996 Ontario census data

The percentage of women reporting having had a screening mammogram in the last two years varies among provinces (Figure 2). Ontario has the highest reported coverage.

Figure 2. Proportion of Canadian women aged 50-69 reporting a screening mammogram within the last two years, National Population Health Survey (NPHS), 1996-1997



Signs and symptoms

More and more breast cancers are now being detected by screening, before the development of symptoms. Symptomatic breast cancer is usually first noticed by the patient as a painless mass. A small proportion of patients report breast pain as the first symptom. Other less common symptoms include thickening, swelling, skin irritation or distortion in shape. Nipple symptoms, including spontaneous discharge, erosion, inversion or tenderness, may also occur. Many of these symptoms are more commonly associated with non-malignant processes, including fibrocystic disease and intraductal papillomas (Ahearne *et al.* 1998). Malaise, bony pain and weight loss are unusual, but may indicate metastatic disease.

Mammographic findings most predictive of malignancy include spiculated masses with associated architectural distortion, clustered micro-calcifications in a linear or branching array, and/or micro-calcifications within a mass (Ahearne *et al.* 1998). While breast cancer may also appear as a round "coin-like" lesion, this is much less common (Henderson 1995).

Diagnosis and staging

The diagnosis of breast cancer typically begins with physical examination, mammography and, sometimes, ultrasound. If appropriate, this is followed by fine-needle aspiration or needle-core biopsy. If the cytologic or histologic findings are not diagnostic, open surgical biopsy is usually undertaken for a definitive diagnosis.

Both breasts are assessed for other lesions, both palpable and non-palpable. Bilateral synchronous cancers may occur in up to 3% of all cases (Ahearne *et al.* 1998).

Treatment of breast cancer requires additional evaluation for the possibility of metastatic disease. A history and physical examination, chest x-ray and evaluation of serum liver enzymes are usually indicated. Additional scans and imaging are not usually warranted unless signs and symptoms are suggestive of metastatic disease. Removal and pathologic examination of the axillary lymph nodes is standard, as it provides accurate staging and prognostic information.

Typically, breast cancer is staged using guidelines from the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Based on clinical and pathologic assessment of tumour size and extension, involvement of regional lymph nodes and the presence or absence of distant metastases, this information is very important for subsequent treatment decisions and for estimating prognosis.

While the OCR does not routinely collect stage information, past comparisons suggest that the stage distribution reported by the Surveillance, Epidemiology and End Results (SEER) system in the US is a reasonable approximation for Ontario, as shown in Table 3 (National Cancer Institute 1999; American Joint Committee on Cancer 1988).

Table 3. Comparison of stage distribution[1] in OCR[2] versus SEER[3]

AJCC[4] summary stage	OCR cases (1988-1991) n=150 (%)	SEER cases (1988-1991) n=52,324 (%)	SEER (1996) n=14,337 (%)
Stage I	39.1	40.9	46.6
Stage II	38.5	38.7	35.0
Stage III	8.6	6.1	6.8
Stage IV	10.1	5.1	4.5
Unknown	3.6	9.3	7.1

[1] Cases are restricted to malignant breast cancer, as the first or only primary. OCR cases were derived from a recent Ontario-wide validation study

[2] Ontario Cancer Registry

[3] Surveillance, Epidemiology and End Results (US)

[4] American Joint Committee on Cancer

Treatment

Breast cancer can be treated with surgery, radiation, chemotherapy or hormonal therapy. Treatment usually incorporates a combination of modalities, depending on the stage and type of cancer and the patient's age and preferences. Canadian guidelines for the treatment of breast cancer are published in appropriate formats for women and for the professionals caring for them (The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer 1998). Breast cancer management guidelines developed by Cancer Care Ontario are available to professionals and the public through CCO's website at www.cancercare.on.ca.

Surgery is the primary treatment for breast cancer. This can be either a partial mastectomy (removing the tumour and a small margin of surrounding normal tissue) or a modified radical mastectomy (removing the entire breast). Long-term survival is similar after both types of surgery and there is some evidence of superior quality of life with partial mastectomy. In 1995-1996, approximately 62% of all Ontario women having surgery for breast cancer had partial mastectomies (sometimes called segmental mastectomy, lumpectomy, wide excision, tylectomy, quadrantectomy or breast conserving surgery). There is considerable geographic variation in breast conserving surgery rates, not only in Ontario, but also in the US and Europe (Iscoe *et al.* 1994).

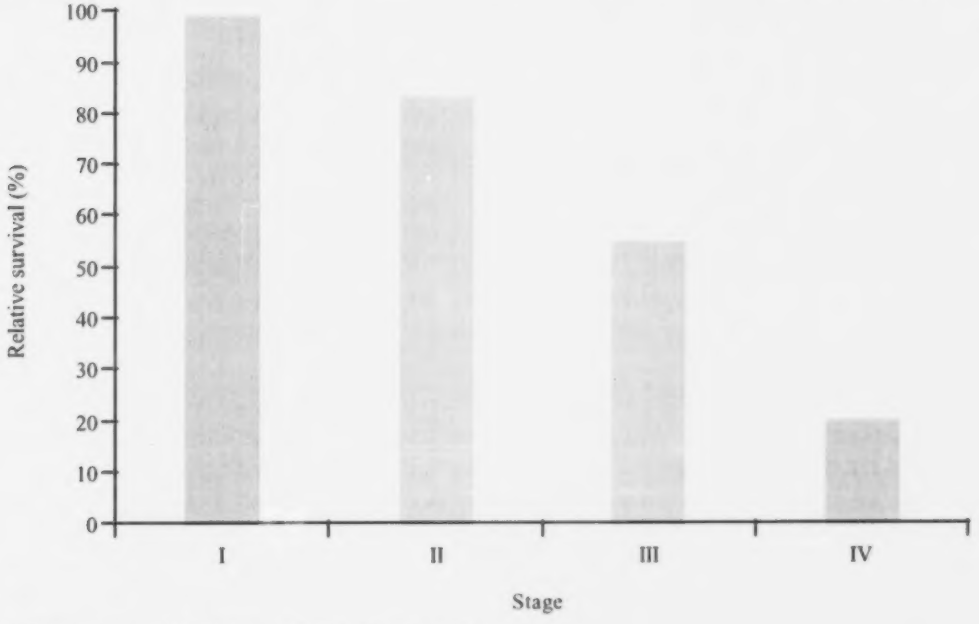
Systemic treatment with chemotherapy or tamoxifen has similar effects on recurrence and survival rates for both axillary node-negative and node-positive breast cancer. Tamoxifen is most effective in postmenopausal women, and chemotherapy in premenopausal women. Systemic treatment is usually recommended for women with node-positive disease because they have a high risk of recurrence, 75-80% over a 10-year period.

Radiation therapy markedly reduces the risk of local recurrence when it is used as an adjuvant after breast conserving surgery. This radiation therapy requires daily outpatient treatments over five to six weeks. Radiation therapy is also useful for palliation in advanced cases of breast cancer, controlling symptoms associated with metastases.

Prognosis

Prognosis is closely related to stage of breast cancer at diagnosis. The US SEER system provides reasonable approximations of survival estimates following breast cancer in Ontario. Figure 3 shows the five-year relative survival rate by stage for cases diagnosed 1990-1991 (National Cancer Institute 1999).

Figure 3. Five-year relative survival, by stage, for US SEER[1] breast cancer cases, 1990-1991



[1] Surveillance, Epidemiology and End Results (US)

Breast Cancer in Ontario 1971-1996

Incidence and Mortality

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Most common cancers and cancer causes of death

In 1992-1996, breast cancer was the commonest cancer diagnosed among Ontario women, representing 29% of the total cancers, and ranked first for every age group (Table 4, Table 5). Breast cancer was also the commonest cause of cancer death among Ontario women, accounting for 19% of all cancer deaths. However, in 1996, lung cancer passed breast cancer as the most common cause of cancer death among Ontario women.

Table 4. Most common cancers diagnosed and cancer causes of death in Ontario females[1], 1992-1996

	Cancer cases				Cancer deaths		
Rank	**Site**	**#**	**%**	**Rank**	**Site**	**#**	**%**
1	Breast	30,378	28.6	1	Breast	9,489	19.4
2	Colon/rectum	13,689	12.9	2	Lung	9,422	19.3
3	Lung	12,210	11.5	3	Colon/rectum	5,162	10.5
4	Corpus uteri	5,772	5.4	4	Ovary	2,570	5.3
5	Ovary	4,570	4.3	5	Pancreas	2,556	5.2
6	Non-Hodgkin's lymphoma	4,109	3.9	6	Non-Hodgkin's lymphoma	1,875	3.8
7	Melanoma	2,995	2.8	7	Leukemia	1,641	3.4
8	Cervix	2,897	2.7	8	Stomach	1,317	2.7
9	Leukemia	2,819	2.7	9	Brain	1,082	2.2
10	Pancreas	2,598	2.4	10	Multiple myeloma	938	1.9
All other sites		24,051	22.7	All other sites		12,884	26.3
Total		**106,088**	**100.0**	**Total**		**48,936**	**100.0**

[1] Non-melanoma skin cancer is not included as it is not recorded in the OCR

Table 5. Ranking of breast cancer cases and deaths relative to other cancers in Ontario women, by age group, 1992-1996

	Cases			Deaths		
Age group	**Rank**	**#**	**%[1]**	**Rank**	**#**	**%[1]**
20-39	1	1,923	24.9	1	340	27.8
40-49	1	5,330	43.7	1	1,062	33.5
50-69	1	13,390	32.0	2	3,708	21.4
70+	1	9,718	22.5	2	4,376	16.2

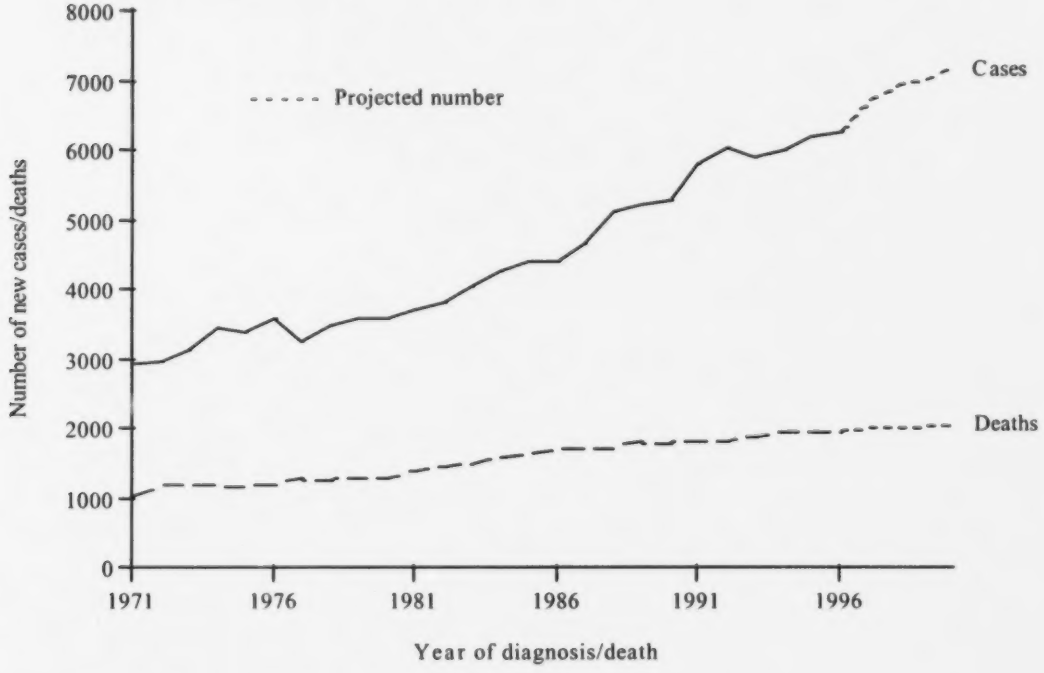
[1] Percentage of all cancers or cancer deaths in the age group

Numbers of new cases and deaths

In the year 2000, approximately 7,200 women in Ontario will be diagnosed with breast cancer. The number of new cases of breast cancer diagnosed annually in Ontario increased by about 3,000 or 113% between 1971 and 1996 (Figure 4). This increase is mainly due to population growth and population aging, rather than an increase in the underlying risk.

In the year 2000 approximately 2,000 Ontario women will die from breast cancer. The number of breast cancer deaths per year also increased over this time period (1971 to 1996) by about 900 cases or about 88%. The number of deaths per year has increased more slowly than the number of new cases. This reflects the steady improvements in survival seen over this time period.

Figure 4. Numbers of new cases of and deaths from breast cancer in Ontario, by year, 1971-1996, and projected to 2000

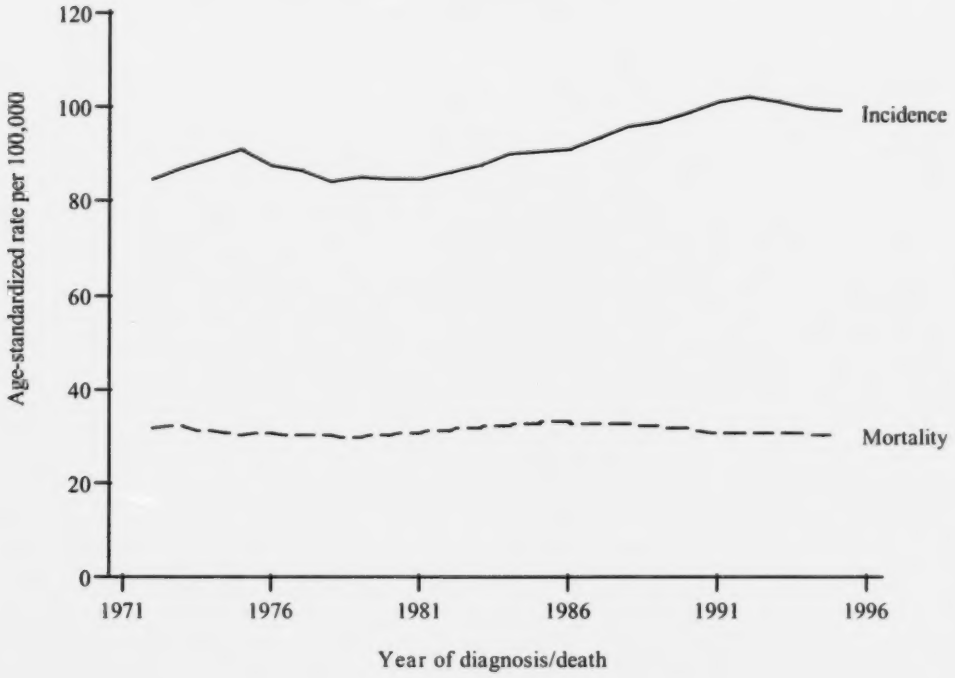


Trends in incidence and mortality

Age-standardized incidence rates for breast cancer increased slowly but steadily from 1971 to 1996 by about 15 per 100,000 or 17% (Figure 5). (Rates are age standardized to the 1991 Canadian population, Appendix A.) This increase may be due, in part, to the rising number of screening mammograms since the mid-1980s and may also be affected by reproductive histories (National Cancer Institute of Canada 2000).

In contrast, age-standardized mortality rates have increased only slightly from 1971 to 1986 (4% increase). Since 1986, mortality has been declining. Between 1986 and 1996 breast cancer mortality in Ontario decreased by about 3 per 100,000 or 9%. This decrease may be due both to improvements in treatment and to the early detection of breast cancers by screening.

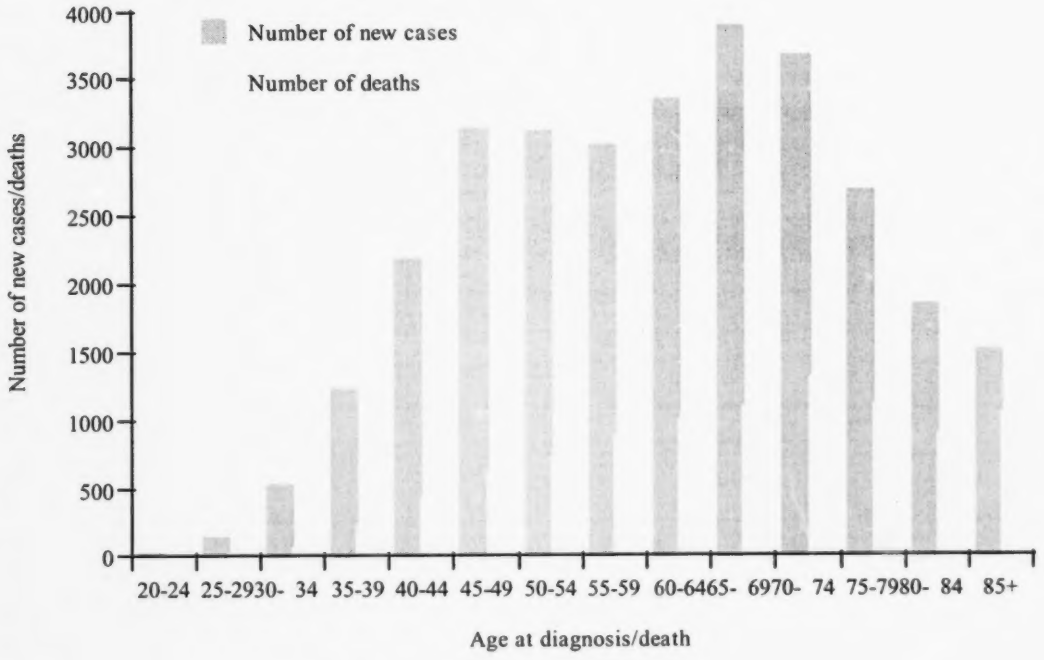
Figure 5. Age-standardized incidence and mortality rates (3-year moving averages) for breast cancer in Ontario, by year, 1971-1996



Numbers of new cases and deaths, by age

The number of newly diagnosed cases increased with age to a peak in the 65-69 age group (Figure 6). The number of breast cancer deaths also increased steadily with age to a peak in the 70-74 age group. Numbers of deaths are considerably less than numbers of new cases in every age group, largely because of the favorable prognosis among the majority of new cases.

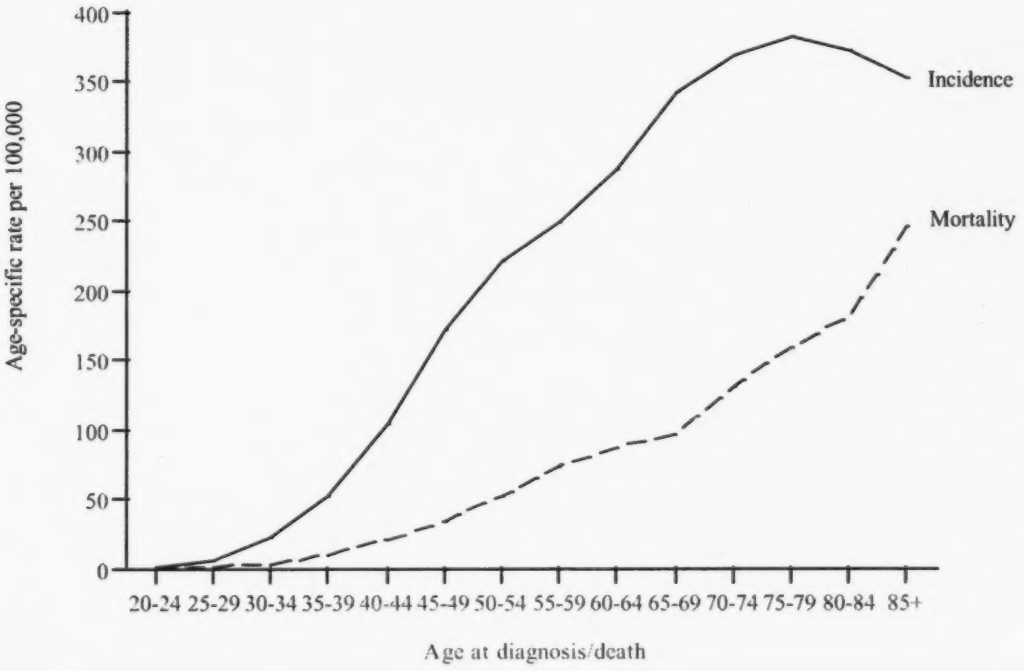
Figure 6. Numbers of new cases of and deaths from breast cancer in Ontario, by age group, 1992-1996



Age-specific incidence and mortality

Breast cancer is very uncommon in women aged less than 30 years and then increases steadily to a peak in the 75-79 age group (Figure 7). Deaths from breast cancer are very uncommon in women aged less than 35 years, but then increase steadily from that age.

Figure 7. Age-specific incidence and mortality rates for breast cancer in Ontario, 1992-1996



Trends in incidence, by age group

For younger women (20-49) incidence rates decreased during the earlier part of the time period (1971-1981) and increased slightly for the later part of the time period (Figure 8, Table 6). This increase may be explained by changes in reproductive histories. For women over 50 years of age incidence rates have increased over the time period, particularly after 1986. This pattern is consistent with the increased use of mammography as a screening test in Canada around this time (National Cancer Institute of Canada 2000).

Figure 8. Age-standardized incidence rates (3-year moving averages) for breast cancer in Ontario, by age group, 1971-1996

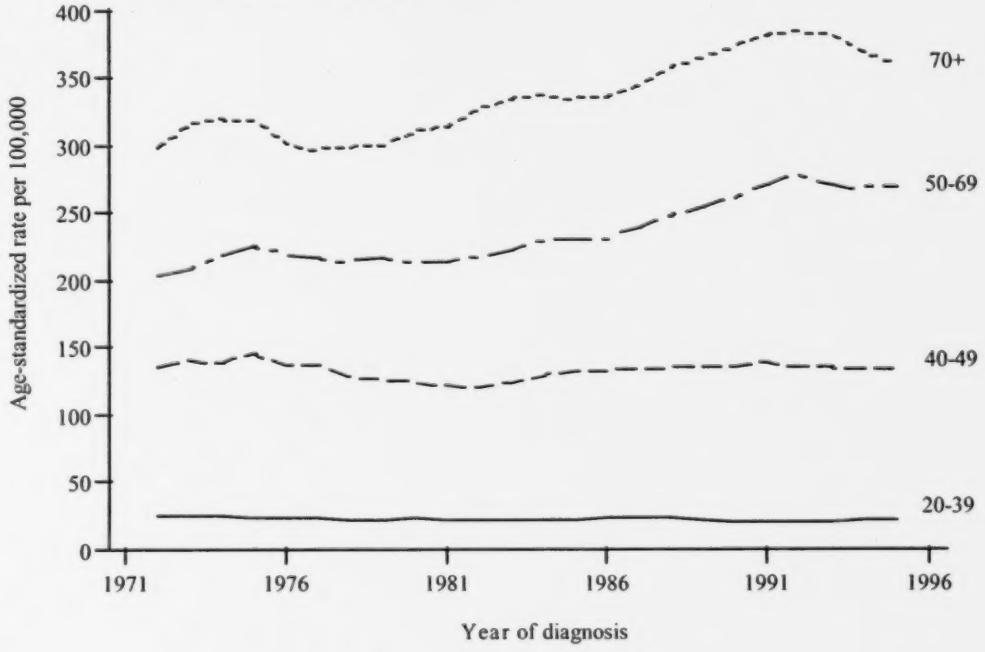


Table 6. Annual percentage change (APC) for breast cancer incidence in Ontario, by age group, 1971-1996

Age group	Period	APC (%)
20-39	1971-1977	-2.2
	1978-1996	0.7
40-49	1971-1981	-1.2
	1982-1996	0.6
50-69	1971-1996	1.4
70+	1971-1996	0.9

Trends in mortality, by age group

Breast cancer mortality rates have been declining for women aged 40-49 since 1971 (Figure 9, Table 7). Mortality rates have been decreasing for women 50-69 since 1989. It is likely that both screening and improved treatments have contributed to this decline. Mortality rates are stable in women under age 40 and are increasing steadily in women age 70 and older.

Figure 9. Age-standardized mortality rates (3-year moving averages) for breast cancer in Ontario, by age group, 1971-1996

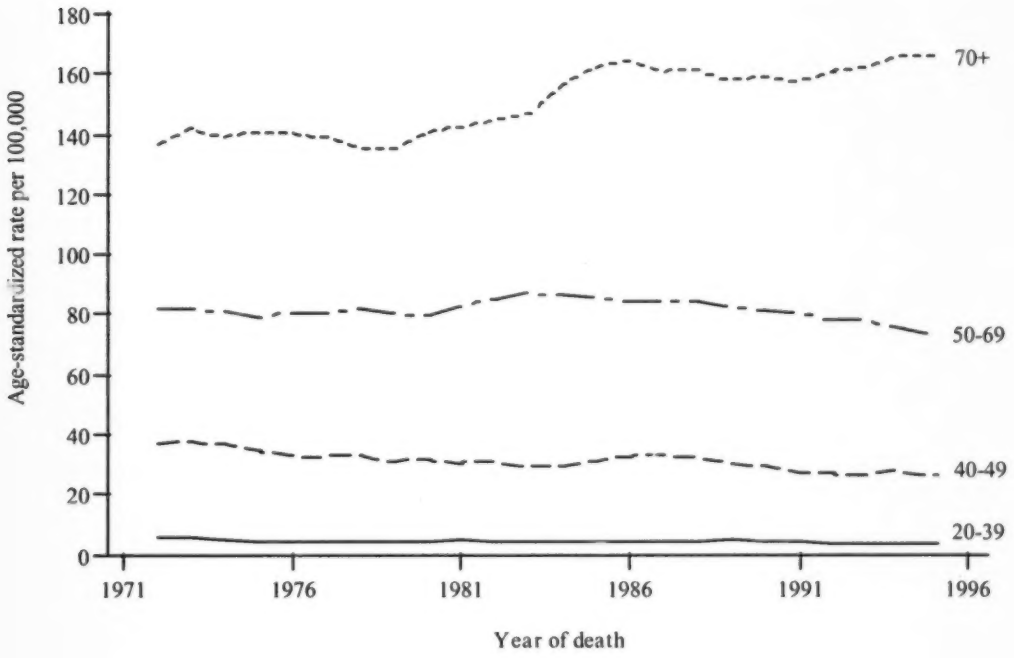


Table 7. Annual percentage change (APC) for breast cancer mortality in Ontario, by age group, 1971-1996

Age group	Period	APC (%)
20-39	1971-1996	0.0
40-49	1971-1996	-1.5
50-69	1971-1988	0.4
	1989-1996	-2.7
70+	1971-1996	0.9

Breast Cancer in Ontario 1971-1996

Geographic Patterns

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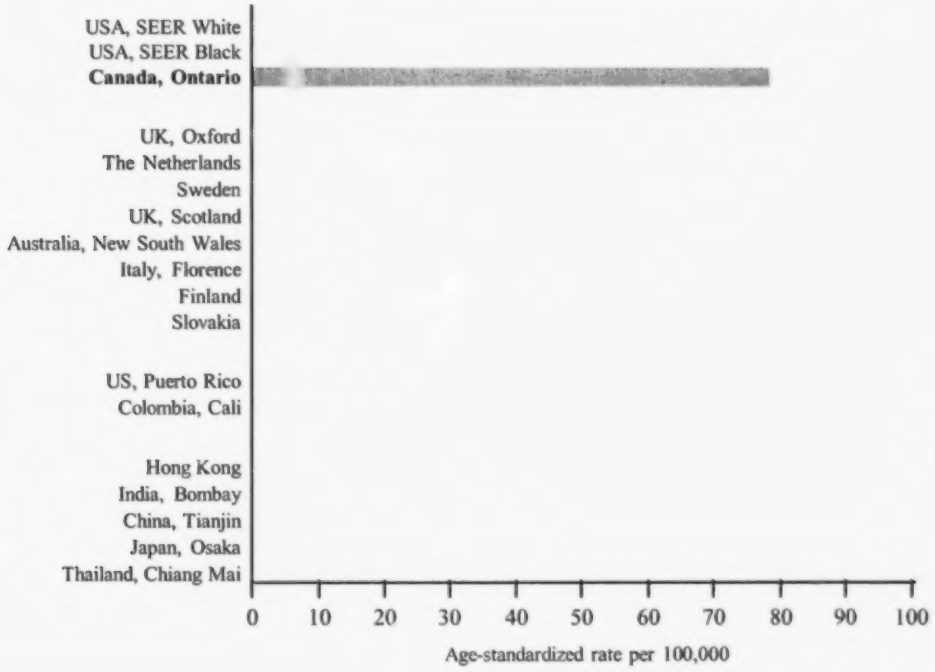
International comparisons

Breast cancer rates vary dramatically around the world. Figure 10 provides examples from some cancer registries with reporting methods similar to Ontario. Breast cancer is generally much commoner in developed countries and lower in developing countries. Breast cancer rates in Ontario (and Canada) are among the highest in the world. These variations are probably due to differences in reproductive patterns, diet, body size and hormone levels.

Figure 10. Age-standardized incidence rates[1] for breast cancer, by country/region, 1988-1992



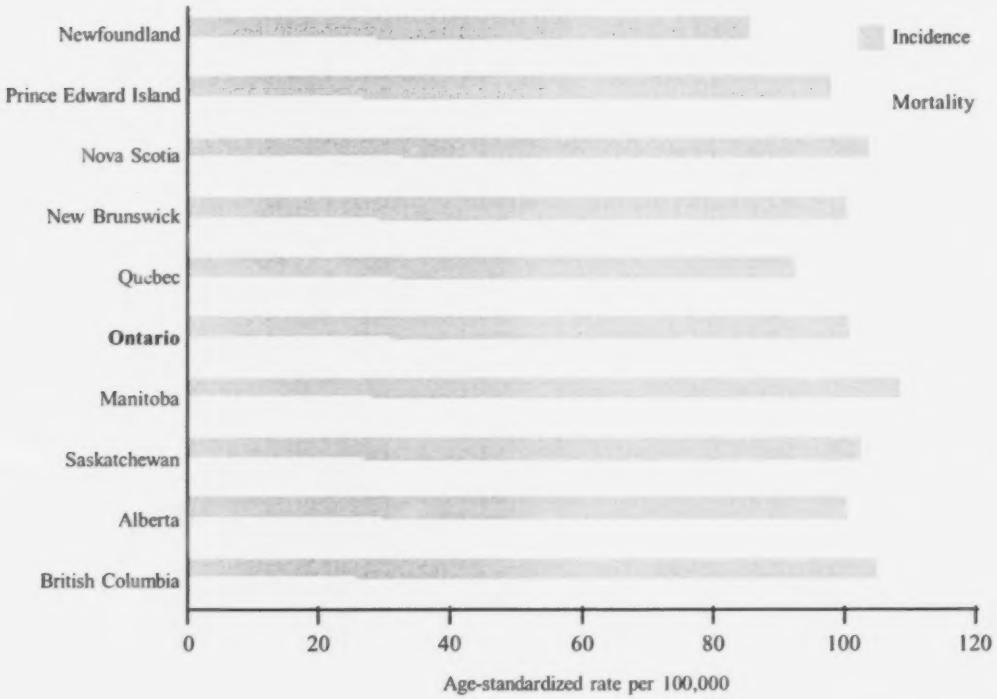
[1] Standardized to the World Standard population

Interprovincial comparisons

There is some variation in breast cancer incidence and mortality rates across Canada (Figure 11). Ontario's incidence and mortality rates for the period 1991-1995 were similar to the Canadian rates, which were 101.8 per 100,000 for incidence and 29.6 per 100,000 for mortality.

In theory, it should be possible to draw inferences about the effectiveness of treatment from the relative levels of incidence and mortality between provinces. This type of analysis should only be undertaken with great caution, however, because of the differences in cancer incidence reporting procedure used by provincial cancer registries.

Figure 11. Age-standardized[1] incidence and mortality rates for breast cancer in Canada, 1991-1995[2]



[1] Standardized to the 1991 Canadian population

[2] For Quebec, incidence data are for 1991-1994

Ontario comparisons

Age-standardized incidence rates for 1992-1996 ranged from 97.6 and 97.7 per 100,000 in the Southwest and South Cancer Care Ontario Regions (CCORs), respectively, to 106.7 in the Eastern CCOR, only a 9% difference (Table 8). (Definitions of the CCORs are found in Appendix B.) Mortality showed a broader range, with the highest rate in the Central West CCOR, at 32.3 per 100,000 and the lowest mortality rate in the Northwest CCOR, at 26.0 per 100,000.

Table 9 and Figure 12 present the age-standardized incidence rates for Ontario's 37 Public Health Units (PHUs) for the time period 1992-1996. (Definitions of the PHUs are found in Appendix C.) Incidence rates ranged from a high of 112.2 per 100,000 in North Bay and District to a low of 71.9 in Huron, a 56% difference.

Table 10 and Figure 13 present age-standardized mortality rates by PHU for 1992-1996. Rates ranged from a high of 36.3 per 100,000 in Leeds-Granville-Lanark to a low of 22.6 per 100,000 in Lambton.

Drawing conclusions about differences in incidence and mortality patterns must be done with caution. Survival rates for breast cancer are high compared with other cancers; this increases the possibility that women may reside in a different area at their time of death than when they are diagnosed.

Table 8. Age-standardized[1] incidence and mortality rates (per 100,000), rate ratios[2] (RR) and 95% confidence intervals (CI) for breast cancer, by CCOR, 1992-1996

	Incidence				Mortality			
CCOR	**#**	**Rate**	**RR**	**95% CI**	**#**	**Rate**	**RR**	**95% CI**
Eastern	3,196	106.7	1.07*	(1.04, 1.11)	983	31.4	1.04	(0.98, 1.11)
Southeast	2,015	101.2	1.02	(0.98, 1.07)	665	31.7	1.05	(0.97, 1.14)
Central East	13,409	97.9	0.99	(0.97, 1.00)	4,053	29.2	0.97*	(0.94, 1.00)
Central West	3,921	98.9	1.00	(0.97, 1.03)	1,355	32.3	1.07*	(1.02, 1.13)
Southwest	4,226	97.6	0.98	(0.95, 1.01)	1,355	29.5	0.98	(0.93, 1.03)
South	984	97.7	0.98	(0.92, 1.05)	331	31.7	1.05	(0.94, 1.17)
Northeast	1,663	97.9	0.99	(0.94, 1.03)	531	30.7	1.02	(0.93, 1.11)
Northwest	683	102.5	1.03	(0.96, 1.11)	178	26.0	0.86*	(0.74, 1.00)
All Ontario[3]	**30,097**	**99.3**	**1.00**		**9,451**	**30.1**	**1.00**	

[1] Standardized to the 1991 Canadian population

[2] Ratio of the incidence or mortality rate in a CCOR to that for all Ontario (known residence only)

[3] Excludes cases and deaths with unknown residence

* Significantly different from 1.0 ($p<0.05$)

Table 9. Age-standardized[1] incidence rates (per 100,000), rate ratios[2] (RR) and 95% confidence intervals (CI) for breast cancer, by Public Health Unit, 1992-1996

		Incidence		
Public Health Unit	**#**	**Rate**	**RR**	**95% CI**
Algoma	358	94.5	0.95	(0.86, 1.05)
Brant	374	107.5	1.08	(0.98, 1.20)
Bruce-Grey-Owen Sound	506	100.2	1.01	(0.92, 1.10)
Durham	983	93.0	0.94*	(0.88, 1.00)
Eastern Ontario	556	103.7	1.04	(0.96, 1.13)
Elgin-St. Thomas	223	94.1	0.95	(0.83, 1.08)
Haldimand-Norfolk	300	98.5	0.99	(0.88, 1.11)
Haliburton-Kawartha-Pine Ridge	509	91.5	0.92	(0.84, 1.01)
Halton	970	104.7	1.05	(0.99, 1.12)
Hamilton-Wentworth	1,402	99.2	1.00	(0.95, 1.05)
Hastings-Prince Edward	474	100.1	1.01	(0.92, 1.10)
Huron	144	71.9	0.72*	(0.61, 0.85)
Kent-Chatham	330	98.3	0.99	(0.89, 1.10)
Kingston-Frontenac-Lennox-Addington	536	102.7	1.03	(0.95, 1.13)
Lambton	368	93.4	0.94	(0.85, 1.04)
Leeds-Grenville-Lanark	496	100.0	1.01	(0.92, 1.10)
Middlesex-London	1,141	102.6	1.03	(0.97, 1.10)
Muskoka-Parry Sound	266	85.5	0.86*	(0.76, 0.97)
Niagara	1,305	97.7	0.98	(0.93, 1.04)
North Bay and District	286	112.2	1.13*	(1.00, 1.27)
Northwestern	201	92.2	0.93	(0.81, 1.07)
Ottawa-Carleton	2,160	109.0	1.10*	(1.05, 1.15)
Oxford	311	106.7	1.07	(0.96, 1.20)
Peel	1,775	97.3	0.98	(0.93, 1.03)
Perth	225	99.1	1.00	(0.87, 1.14)
Peterborough	427	101.4	1.02	(0.92, 1.12)
Porcupine	194	81.8	0.82*	(0.71, 0.95)
Renfrew	311	106.0	1.07	(0.95, 1.19)
Simcoe	917	101.2	1.02	(0.95, 1.09)
Sudbury and District	586	103.8	1.04	(0.96, 1.13)
Thunder Bay	482	107.7	1.08	(0.99, 1.19)
Timiskaming	112	92.1	0.93	(0.76, 1.12)
Toronto	7,002	97.5	0.98	(0.96, 1.01)
Waterloo	978	94.2	0.95	(0.89, 1.01)
Wellington-Dufferin-Guelph	540	95.2	0.96	(0.88, 1.04)
Windsor-Essex	984	97.7	0.98	(0.92, 1.05)
York	1,365	100.6	1.01	(0.96, 1.07)
All Ontario[3]	**30,097**	**99.3**	**1.00**	

[1] Standardized to the 1991 Canadian population

[2] Ratio of the incidence rate in a Public Health Unit to that for all Ontario (known residence only)

[3] Excludes cases with unknown residence

* Significantly different from 1.0 ($p<0.05$)

Figure 12. Age-standardized incidence rates for breast cancer, by Public Health Unit, 1992-1996

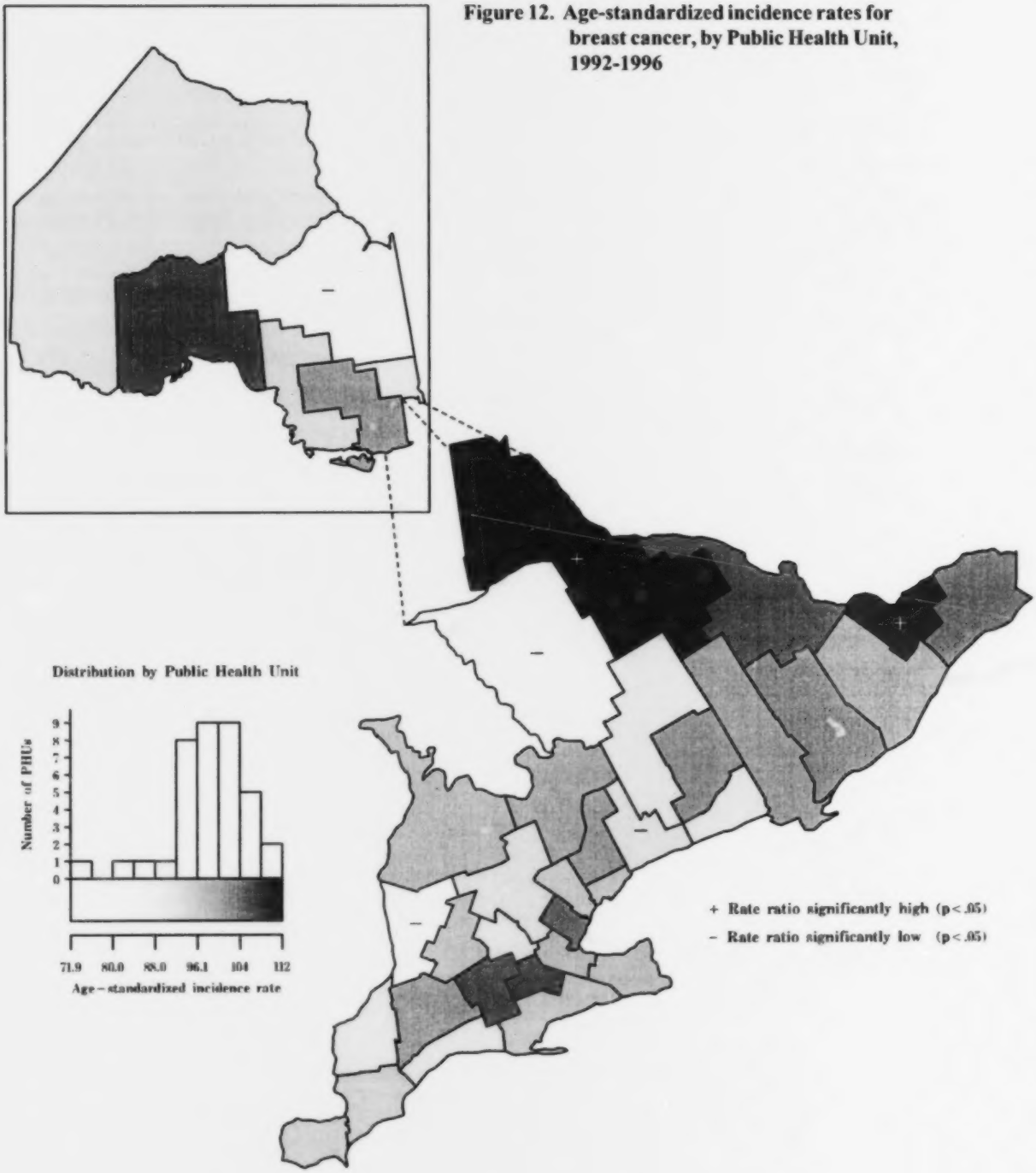


Table 10. Age-standardized mortality rates (per 100,000), rate ratios[2](RR) and 95% confidence intervals (CI) for breast cancer, by Public Health Unit, 1992-1996

		Mortality		
Public Health Unit	**#**	**Rate**	**RR**	**95% CI**
Algoma	115	30.0	1.00	(0.82, 1.19)
Brant	108	28.8	0.96	(0.78, 1.16)
Bruce-Grey-Owen Sound	168	31.7	1.05	(0.90, 1.23)
Durham	277	26.9	0.89	(0.79, 1.00)
Eastern Ontario	159	27.6	0.92	(0.78, 1.07)
Elgin-St. Thomas	77	29.8	0.99	(0.78, 1.24)
Haldimand-Norfolk	99	30.9	1.02	(0.83, 1.25)
Haliburton-Kawartha-Pine Ridge	161	26.7	0.89	(0.76, 1.04)
Halton	318	34.7	1.15*	(1.03, 1.28)
Hamilton-Wentworth	502	33.3	1.10*	(1.01, 1.20)
Hastings-Prince Edward	161	32.4	1.07	(0.91, 1.26)
Huron	57	27.7	0.92	(0.70, 1.20)
Kent-Chatham	114	31.6	1.05	(0.87, 1.26)
Kingston-Frontenac-Lennox-Addington	182	33.0	1.09	(0.94, 1.26)
Lambton	96	22.6	0.75*	(0.61, 0.91)
Leeds-Grenville-Lanark	194	36.3	1.20*	(1.04, 1.39)
Middlesex-London	397	34.4	1.14*	(1.03, 1.26)
Muskoka-Parry Sound	112	33.0	1.10	(0.90, 1.32)
Niagara	470	33.5	1.11*	(1.01, 1.22)
North Bay and District	93	35.3	1.17	(0.95, 1.43)
Northwestern	58	26.1	0.87	(0.66, 1.12)
Ottawa-Carleton	660	32.6	1.08	(1.00, 1.17)
Oxford	90	26.4	0.88	(0.70, 1.08)
Peel	476	27.8	0.92	(0.84, 1.01)
Perth	69	28.0	0.93	(0.72, 1.18)
Peterborough	123	28.7	0.95	(0.79, 1.14)
Porcupine	67	28.2	0.94	(0.73, 1.18)
Renfrew	94	29.6	0.98	(0.79, 1.20)
Simcoe	290	31.3	1.04	(0.92, 1.17)
Sudbury and District	163	28.7	0.95	(0.81, 1.11)
Thunder Bay	120	26.0	0.86	(0.72, 1.03)
Timiskaming	41	33.2	1.10	(0.80, 1.49)
Toronto	2,182	28.9	0.96	(0.92, 1.00)
Waterloo	287	26.8	0.89*	(0.79, 1.00)
Wellington-Dufferin-Guelph	176	30.9	1.03	(0.88, 1.19)
Windsor-Essex	331	31.7	1.05	(0.94, 1.17)
York	364	28.6	0.95	(0.85, 1.05)
All Ontario[3]	**9,451**	**30.1**	**1.00**	

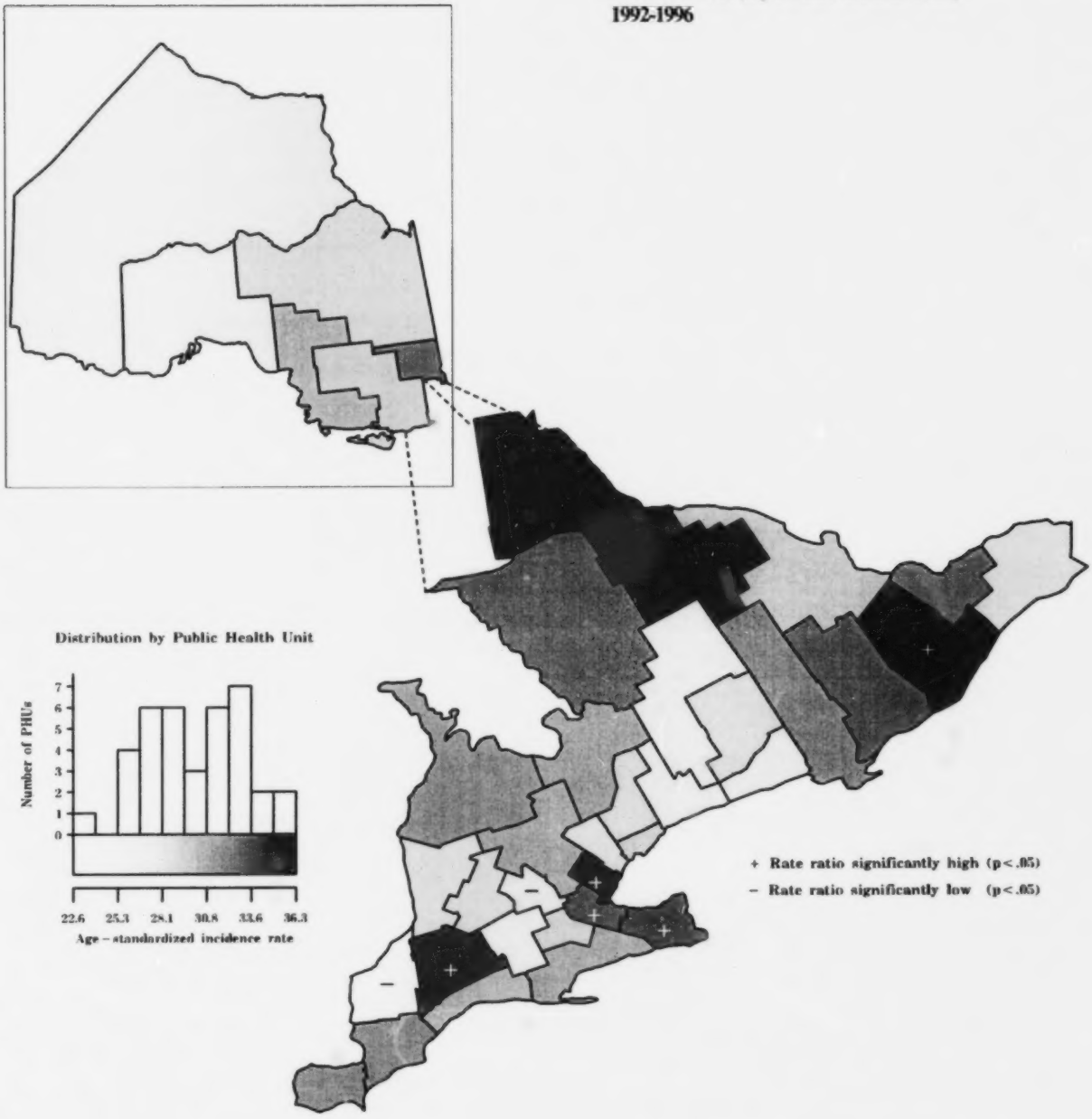
[1] Standardized to the 1991 Canadian population

[2] Ratio of the mortality rate in a Public Health Unit to that for all Ontario (known residence only)

[3] Excludes deaths with unknown residence

* Significantly different from 1.0 ($p<0.05$)

Figure 13. Age-standardized mortality rates for breast cancer, by Public Health Unit, 1992-1996



Breast Cancer in Ontario 1971-1996

Morphology

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Morphologic patterns, by age group

Infiltrating duct carcinoma accounts for 70% of newly diagnosed breast cancer cases at all ages (Table 11). The percentage is relatively constant across the age groupings. These percentages are likely underestimates, because breast cancers with non-specific diagnoses of adenocarcinoma and carcinoma, while classified separately, would most likely prove to be duct carcinoma if more or better tissue had been available, or if the pathologist had been more precise (Berg and Hutter 1995).

Infiltrating lobular carcinoma and coincident infiltrating duct and lobular carcinoma comprise the second and third most common morphologic subgroups of breast cancer. The highest proportion of lobular carcinoma is in the oldest age group, while the proportions are similar across all age groups for coincident infiltrating duct and lobular carcinoma.

The next most common morphologic subgroups are comedocarcinoma, mucinous adenocarcinoma and medullary carcinoma. Medullary carcinoma and comedocarcinoma are more common in the youngest age groups and mucinous adenocarcinoma is more common in the oldest age group.

Table 11. Percentage distribution of morphologic subgroups for breast cancer in Ontario, by age group, 1992-1996

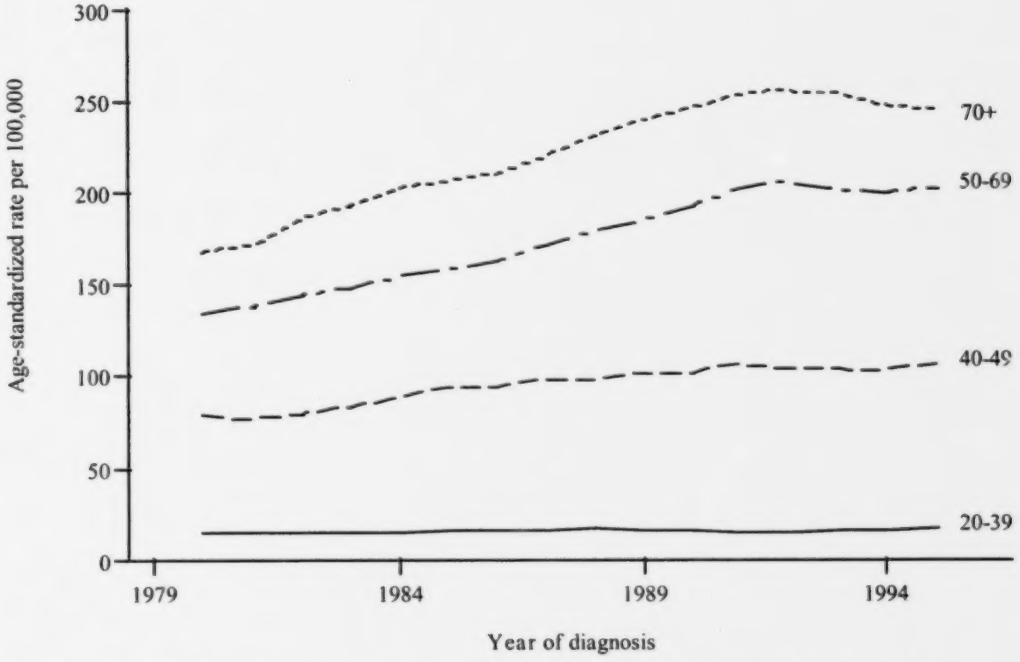
	All ages[1]		20-39		40-49		50-69		70+	
	#	%	#	%	#	%	#	%	#	%
Infiltrating duct carcinoma	21,114	69.5	1,404	73.0	3,972	74.5	9,519	71.1	6,210	63.9
Infiltrating lobular carcinoma	2,474	8.1	78	4.1	339	6.4	1,191	8.9	864	8.9
Infiltrating duct and lobular carcinoma	1,126	3.7	76	4.0	212	4.0	537	4.0	301	3.1
Comedocarcinoma	692	2.3	67	3.5	157	2.9	342	2.6	126	1.3
Mucinous adenocarcinoma	508	1.7	20	1.0	45	0.8	181	1.4	262	2.7
Medullary carcinoma	451	1.5	72	3.7	131	2.5	177	1.3	71	0.7
Paget's disease	344	1.1	19	1.0	46	0.9	153	1.1	126	1.3
Other carcinoma	2,222	7.3	129	6.7	321	6.0	967	7.2	800	8.2
Other/specified morphology	127	0.4	24	1.2	35	0.7	40	0.3	28	0.3
Unspecified morphology	1,320	4.3	34	1.8	72	1.4	283	2.1	930	9.6
Total	**30,378**	**100.0**	**1,923**	**100.0**	**5,330**	**100.0**	**13,390**	**100.0**	**9,7181**	**00.0**

[1] Totals across age groups may be less than the total for all ages because there are a few women under age 20 or of unknown age

Trends in incidence for infiltrating duct carcinoma, by age

Figure 14 shows incidence rates for infiltrating duct carcinoma according to age at diagnosis. There has been a steady increase in the incidence rates for each age group, although somewhat less so for women aged 20-39 years at diagnosis.

Figure 14. Age-standardized incidence rates (3-year moving averages) for infiltrating duct carcinoma[1] of the breast in Ontario, by age group, 1979-1996

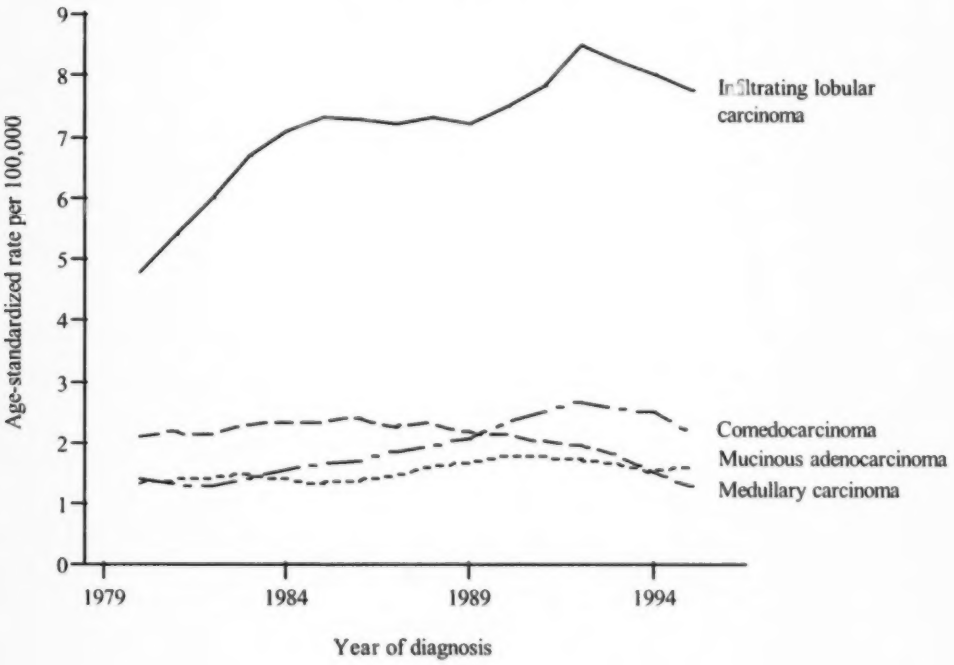


[1] Includes infiltrating duct and lobular carcinoma (ICDO-2 (International Classification of Diseases for Oncology, 2nd edition) code 8522)

Trends in incidence, by morphologic subgroup

Incidence trends over time for common breast cancer morphologic subgroups are shown in Figure 15. For lobular carcinoma, the rate of increase in incidence resembles that seen for infiltrating duct carcinoma, with a similar leveling of incidence rates in recent years. Incidence rates are progressively increasing for comedocarcinoma and mucinous adenocarcinoma. The incidence rate for medullary carcinoma, however, has been falling steadily, especially since the late 1980s.

Figure 15. Age-standardized incidence rates (3-year moving averages) for breast cancer in Ontario, by morphologic subgroup, 1979-1996



Breast Cancer in Ontario 1971-1996

Survival

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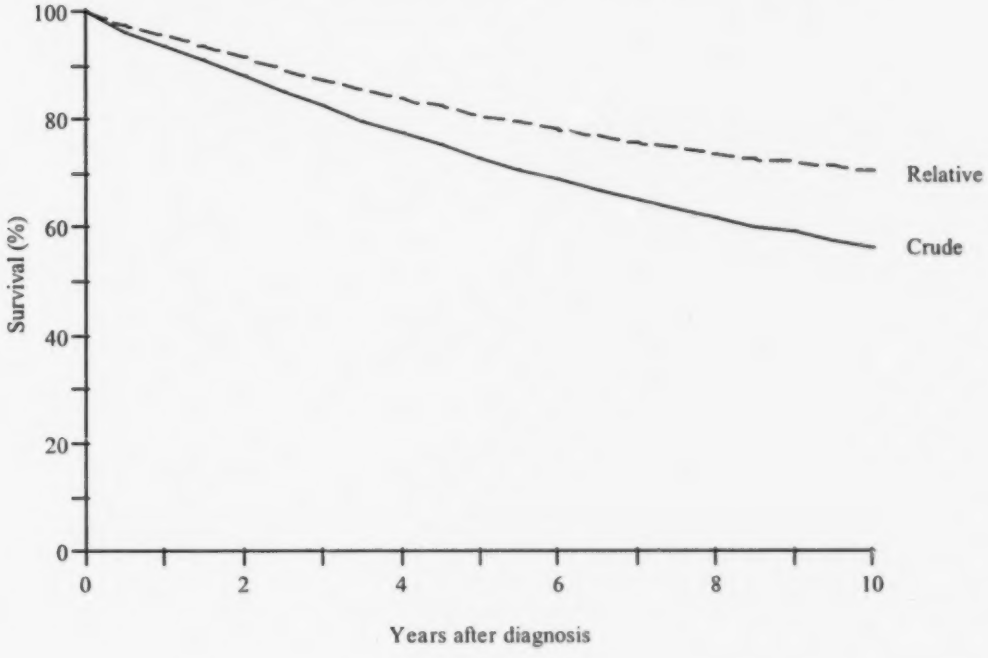
Crude and relative survival

Survival rates for breast cancer are higher than those for most other cancers (McLaughlin *et al.* 1995). The one-year relative survival rate after diagnosis of breast cancer is 96% and the five-year relative survival is 81% (Figure 16). Relative survival declined a further 10% to 71% at 10 years.

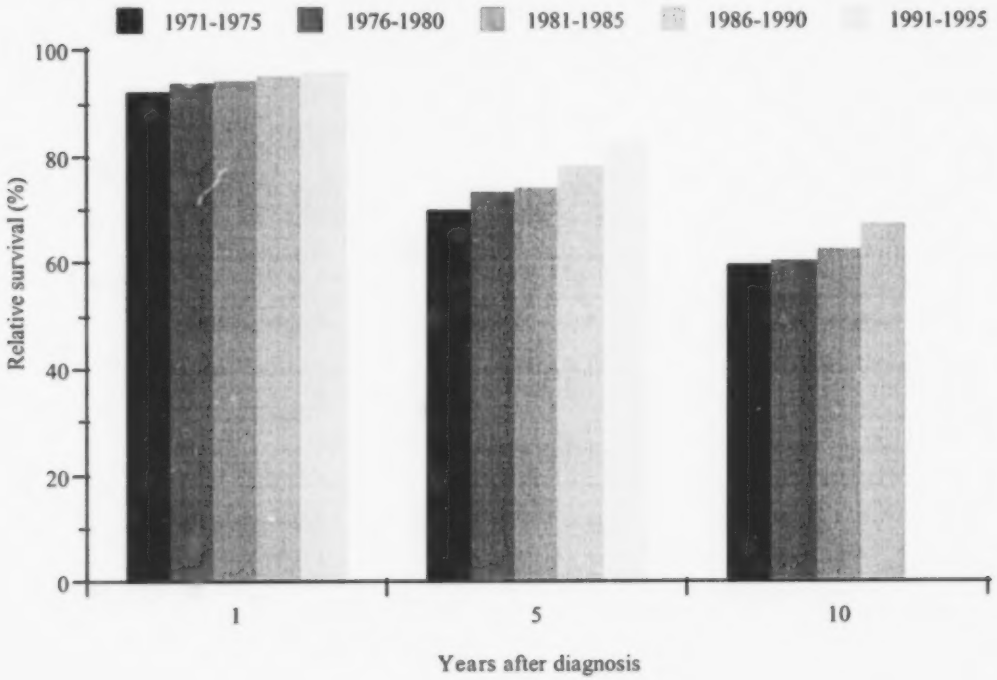
Figure 16. Crude and relative survival for breast cancer in Ontario, 1987-1996



Relative survival, by period of diagnosis

Relative survival after diagnosis of breast cancer has been improving over time (Figure 17). The largest improvements in survival occurred during the 1980s. This may partially be explained by the improved effectiveness of treatment, such as the introduction of adjuvant treatment (chemotherapy for premenopausal women and tamoxifen for postmenopausal women) in the early to mid-1980s (Olivotto *et al.* 1994). In recent years, earlier detection by screening may have contributed to improvements in survival.

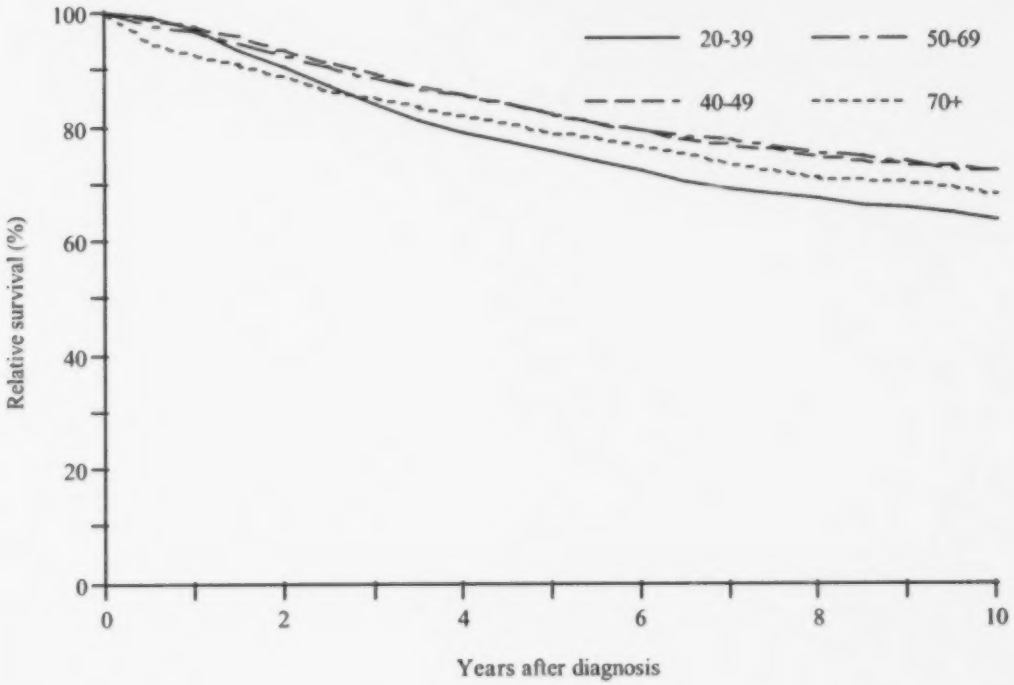
Figure 17. Relative survival for breast cancer in Ontario, by period of diagnosis, 1971-1995



Relative survival, by age group

Relative survival showed little variation by age at diagnosis (Figure 18). The highest relative survival is for women diagnosed at age 40-49 and 50-69, with a five-year relative survival of 82%. Women diagnosed at age 20-39 have slightly lower survival rates, with a five-year relative survival rate of 76%. This pattern may be explained by other known prognostic factors such as menopausal status and age differences in estrogen receptor status and stage of disease at diagnosis (Lees 1989; Merkel and Osborne 1989).

Figure 18. Relative survival for breast cancer in Ontario, by age group, 1987-1996



Relative survival, by morphologic subgroup

Women with infiltrating duct carcinoma have a lower five- and 10-year relative survival than women with special types of carcinomas, a pattern that is consistent with previous reports (Berg and Hutter 1995) (Table 12). Special-type carcinomas such as lobular and mucinous have the best five-year relative survival rates and medullary and mucinous have the best 10-year survival rates. The differences in survival rate may reflect the stage at which the cancer was diagnosed in the different types of carcinomas (Berg and Hutter 1995).

Table 12. Relative survival (%) and 95% confidence intervals (CI) for breast cancer in Ontario, by morphologic subgroup, 1979-1996

		5-year		10-year	
	#	%	95% CI	%	95% CI
Infiltrating duct carcinoma[1]	57,536	80.0	(79.6, 80.5)	67.0	(66.4, 67.6)
Infiltrating lobular carcinoma	6,320	85.5	(84.2, 86.7)	71.2	(69.3, 73.1)
Medullary carcinoma	1,721	82.5	(80.4, 84.7)	77.5	(74.7, 80.3)
Comedocarcinoma	1,683	82.7	(80.5, 85.0)	73.0	(69.8, 76.3)
Mucinous adenocarcinoma	1,374	91.2	(88.4, 94.1)	83.5	(78.8, 88.3)

[1] Includes infiltrating duct and lobular carcinoma (ICDO-2 (International Classification of Diseases for Oncology, 2nd edition) code 8522)

Breast Cancer in Ontario 1971-1996

Materials and Methods /References /Appendices

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Materials and Methods

Data sources

New cases of cancer

The Ontario Cancer Registry (OCR), operated by Cancer Care Ontario (CCO), registers all newly diagnosed cases of cancer (invasive neoplasms) except non-melanoma skin cancers. While cancer reporting is not a legal requirement in Ontario, the Cancer Act provides a legal mandate for this undertaking and offers legal protection for physicians, dentists and health care agencies which report information on cancer cases.

The process of cancer registration in Ontario is passive, relying almost completely on records collected for other purposes. Since 1977, the OCR has relied on the same four major data sources: hospital discharge summaries which include a diagnosis of cancer; pathology reports with any mention of cancer; records of patients referred to CCO's eight Regional Cancer Centres (RCCs) or the Princess Margaret Hospital (PMH) (now part of the University Health Network), the specialized institutions treating cancer patients in Ontario; and death certificates with cancer as the underlying cause of death.

All records except pathology reports are coded at the source and provided to the OCR in machine-readable form. Paper copies of pathology reports are sent to the OCR by all hospital and private pathology laboratories and are coded and key-entered by OCR staff. Since 1991, the OCR has also received day surgery summaries which include a diagnosis of cancer. The OCR receives about 400,000 records from these multiple sources each year. The OCR is highly automated, relying heavily on automated edit-checking, computerized probabilistic record linkage and automated rule-based systems for summarizing patient and tumour information. Further details about the operation are available in recent monographs (Holowaty *et al.* 1995; Marrett *et al.* 1995; McLaughlin *et al.* 1995).

Quality of data for new cases of cancer

Microscopic examination of tissue or cells is the definitive diagnostic test for cancer. During the period 1971-1996, 7% of breast cancers were not microscopically verified in the OCR. This proportion decreased to under 5% for the more recent interval 1979-1996, largely because of more complete reporting from pathology laboratories. This rate of non-microscopic confirmation is still somewhat above that reported by established active registries; for instance, the American SEER (Surveillance, Epidemiology and End Results Program) registries report a rate of 3%.

Another parameter of data quality is the percentage of cases for which a death certificate is the only source of information supporting a diagnosis of breast cancer. Only 1% of breast cancers registered from 1971-1996 was registered from death certificates only. Figure 19 shows the temporal trends in data quality indicators for breast cancer.

Because the management of breast cancer almost always requires contact with institutions that comprise two or more of the OCR's major reporting sources, it is likely that reporting is almost complete. During the 1971-1996 time period, only 11% of breast cancer cases registered in the OCR were identified by a single source, with 6%, 2%, 2% and 1% of cases, respectively, being identified by hospitalization records, pathology records, clinic records and death certificates only.

Deaths from cancer

Mortality data in the OCR are largely derived from the Office of the Registrar General of Ontario, where death certificate information is collected and coded. Mortality rates are estimated from the

reported underlying cause of death, coded according to the International Classification of Diseases - Ninth Revision (ICD-9), among persons residing in Ontario at the time of death (World Health Organization 1977).

Population data

Rates were calculated using annual mid-year estimated resident populations of females by five-year age group. These estimates are based on the National Population Census, conducted every five years, and are corrected for census undercounts. Populations for both Ontario and its census divisions were provided by Statistics Canada (Statistics Canada 1999). Populations for CCO Regions (CCORs) and Public Health Units (PHUs) were determined by adding the populations for all census divisions that comprise each Region or Unit (see Appendices B and C).

The age distribution of the 1991 Canadian population, adjusted for census undercount, was used to calculate most of the age-standardized rates appearing in this monograph (Statistics Canada 1994) (see Appendix A). For international comparisons, the World Standard Population was used to calculate the age-standardized rates (Parkin *et al.* 1997) (see Appendix A).

National and international data

Incidence and mortality rates for the provinces in Canada were obtained from the North American Association of Central Registries (NAACCR) 1999 Cancer in North America (CINA) monographs (Chen *et al.* 1999; Chen and Wu 1999). The monographs cover the period 1991-1995 for most participating registries. Incidence rates of breast cancer around the world were recently published by the International Agency for Research on Cancer (IARC) (Parkin *et al.* 1997). This monograph covers the period 1988-1992 for most reporting registries. For comparison with Ontario incidence data, countries or regions were selected to represent different continents, but also had to meet all of the data quality requirements of the IARC publication. No areas of Africa qualified for this comparison.

Incidence and mortality data

Cancer site

A cancer is generally coded according to the body site in which it occurs. In the OCR, the primary site of cancer or cancer cause of death has been coded according to ICD-9 (World Health Organization 1977). The ICD-9 code for invasive cancer of the breast is 174. Although this code has a fourth digit which indicates the more specific site of the cancer within the breast (174.0 for the nipple and areola, 174.1 for the central portion, 174.2-174.5 for the quadrants, 174.6 for the axillary tail and 174.8 for overlapping subsites or ectopic sites), this digit was often recorded in the OCR as a '9', which means that no subsite was specified. Therefore, data have been presented only for site 174 as a whole.

Morphology

The microscopic morphology or histopathology of tumours concerns the appearance of cancerous cells, tissues and organs under the light microscope. The morphologic type of a cancer may be a prognostic factor; additionally, it may be important for treatment decisions. It may also be important in epidemiologic studies of cancer etiology. Cancers of different morphologic types that occur in the same anatomic site often have different etiologies, incidences and prognoses.

The morphologic data presented in this monograph have been coded according to the International Classification of Diseases for Oncology (ICD-O) (World Health Organization 1976; Percy *et al.* 1990). The morphology code in ICD-O consists of five digits. The first four digits describe the

morphologic type, and the fifth digit describes the behaviour. The OCR registers only malignant neoplasms; that is, those with a behaviour code of 3.

As the total number of morphologic types recognized in ICD-O approaches 500, grouping of the various types is necessary. Appendix D shows the grouping scheme employed for this monograph, a variant of the histology groups defined by Berg for use in epidemiologic studies (Percy *et al.* 1995; Berg and Hutter 1995). For the most recent five-year time period, we included coincident infiltrating duct and lobular carcinoma as a separate category, but combined it with infiltrating duct carcinoma for analysis of time trends for the period 1979-1996. This reflects coding history in the OCR; prior to 1988, coincident infiltrating duct and lobular carcinoma was coded as infiltrating duct carcinoma.

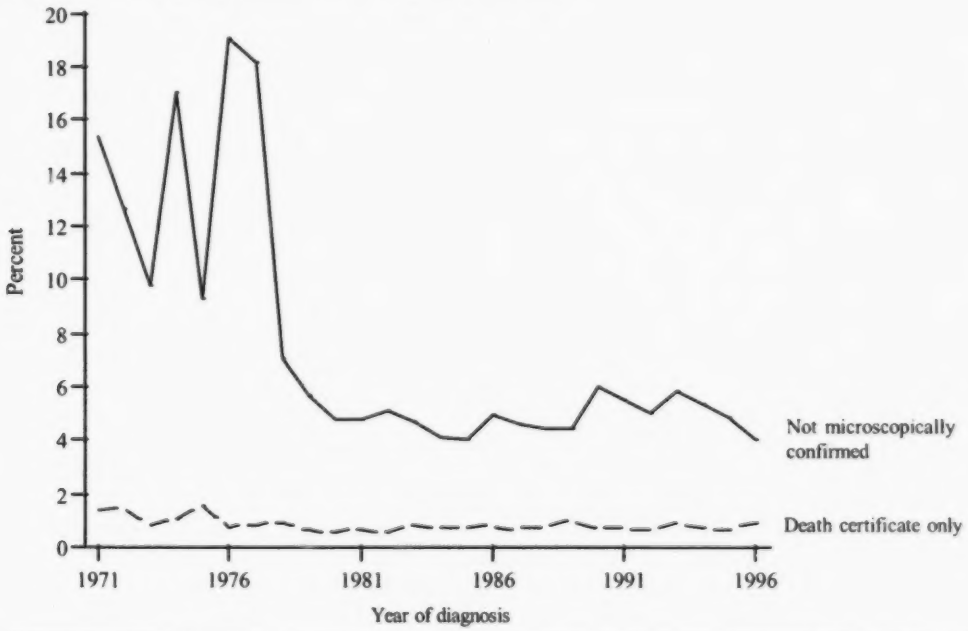
Time periods

Incidence, mortality and survival trends are presented in this monograph for the period 1971-1996. While the OCR actually begins in 1964, population estimates adjusted for census undercount are only available since 1971. The most recent years for which reporting is complete are 1996 for incidence and 1997 for mortality.

The most recent five-year time period, 1992-1996, was used to estimate the burden of cancer and to describe selected characteristics of tumours or cases. This five-year aggregate stabilizes estimates of infrequent events (diagnoses at younger ages, for example) while providing the most current information.

More detailed analyses by morphologic subgroup were focused on the period 1979-1996, because of the appreciable improvement in the rates of microscopic confirmation between 1971 and 1979 (Figure 19). Other periods were used occasionally because of availability; for example, data from other provinces of Canada are for 1991-1995. The most recently published international data are for 1988-1992.

Figure 19. Temporal trends in data quality indicators



Residence at diagnosis and death

The geographic variation in incidence and mortality in breast cancer in Ontario over the period 1992-1996 is described in terms of Cancer Care Ontario Regions (CCORs) and Public Health Units (PHUs), which are aggregations of census divisions (see Appendices B and C). Census division of residence at the time of diagnosis comes primarily from hospital records in the OCR. All but 1% of cases of breast cancer in 1992-1996 have a census division of residence recorded. Cases with missing residence were excluded from all incidence rates calculated for the purpose of comparing the CCORs or PHUs to the province. Census division of residence at time of death comes from death certificates in the OCR. Mortality rates for CCOR and PHU comparisons were also calculated with missing residence excluded; fewer than 1% of breast cancer deaths for the 1992-1996 time period did not report a valid census division of residence.

The eight CCORs cover the entire province, with populations ranging from 5,484,173 in the largest (Central East CCOR) to 373,008 in the smallest (South CCOR) (Statistics Canada 1999). Within each CCOR is situated one of CCO's Regional Cancer Centres. In addition, Princess Margaret Hospital is located within the Central East CCOR. Maps describing CCOR boundaries and census division components are shown in Appendix B.

Appendix C contains a map showing Ontario PHUs and a table showing corresponding census divisions as used for PHU analysis. It should be noted that actual PHU boundaries are not always equivalent to those for the grouped census divisions as used herein. The discrepancy is greatest in northern Ontario. The following PHUs do not correspond exactly to groups of census divisions: Algoma, Muskoka-Parry Sound, North Bay and District, Northwestern, Porcupine, Renfrew, Sudbury and District, Thunder Bay, and Timiskaming.

Statistical methods

Age-specific rates

Age-specific rates were calculated in five-year age groups by dividing the number of cases or deaths by the Ontario female population in the same age group for the same calendar period. Age-specific rates are expressed per 100,000 women-years.

Age-standardized rates

To compare incidence and mortality rates between populations which have different age structures, age-standardized rates were calculated. The age-standardized rate is a weighted average of the age-specific rates, using a standard population age distribution. The standardized rates reflect the incidence and mortality that would be expected if the population of interest had an age structure identical to the standard population. The 1991 Canadian population, adjusted for census undercount (Appendix A), was used as the standard throughout most of this monograph. However, in comparisons between Ontario's rate and those of other parts of the world, the World Standard Population was used (see Appendix A). Age-standardized rates are expressed per 100,000 women-years.

Time trends

The annual numbers of incident cases and deaths were plotted to describe the total burden of breast cancer for the period 1971-1996. To illustrate time trends, three-year moving averages of

age-standardized incidence and mortality rates were plotted, for all ages and by age group. These averages smooth out annual fluctuations that can occur when there are small numbers of cases. Trends by morphologic subgroup were plotted from 1979 to 1996, again using three-year moving averages.

In order to estimate the annual percentage change (APC), the logarithm of the annual rate was modelled as a function of year of diagnosis or death using weighted linear regression and SAS® PROCs REG and GLM (Esteve *et al.* 1994; SAS Institute Inc. 1997). First, the entire time period was modeled, allowing the inclusion of a quadratic year term if necessary. If the quadratic term was found to be significant or if the model fit was poor, a change-point analysis was undertaken to determine the year at which the rate of annual increase or decrease changed markedly (Shaban 1980). In this second step, two lines were fit to the data (one prior to the change point and one after) to try to improve the model; the increase in the percentage of variation explained by the model (R^2) was used to select the best two-line model.

The APC estimates are reported either for the entire time period or for two time periods, depending on the results of the change-point analysis.

Rate ratios

The comparison of incidence or mortality rates in two populations (or subgroups), as a ratio of these rates, is termed a rate ratio (RR) or relative rate. In this monograph, this technique was employed for comparison of the rates of breast cancer for each CCOR or PHU to that of the province as a whole. The rates for each population were age-standardized using the 1991 Canadian population, adjusted for census undercount (Appendix A), as the standard. A rate ratio in excess of 1.0 for regional comparisons, for example, means that the region has a higher rate than Ontario as a whole.

Confidence intervals

A confidence interval (CI) indicates the range of values for a parameter of interest (for example, a rate ratio) which has a specified probability of including the true value. Thus, the 95% CI for a RR represents the interval which has a 95% chance of covering the true value of the RR. The 95% CI for each incidence and mortality RR comparing a regional rate to the provincial rate was calculated using the approximate bootstrap confidence interval method (Swift 1995).

When the 95% CI includes 1.0, the RR is considered not to differ significantly from 1.0 (that is, the rate for the region does not differ significantly from that for the province), and the difference between the RR and 1.0 is ascribed to chance variation. If the interval does not include 1.0, the RR is deemed to be statistically significantly different from 1.0. A RR is declared to be significantly low if the upper limit of the CI is less than 1.0 and significantly high if the lower limit of the CI is greater than 1.0. Due to rounding, a RR may occasionally be declared to differ significantly from 1.0 when one of the end points of the CI is 1.0.

Projections

The expected number of incident cases and deaths from breast cancer are presented up to the year 2000. These estimates were calculated by extrapolating age-specific incidence and mortality rate

trends using data from 1986 to 1996 and applying these extrapolated rates to projected Ontario population estimates made available by the Ontario Ministry of Health and Long Term Care.

Survival

Cases with a first primary diagnosis of breast cancer between 1971 and 1996 were used in the survival analyses for all cases and by age group; the time period 1979-1996 was used for the analyses by morphologic subgroup. Cases were followed for deaths occurring through December 31, 1998 (as recorded in the OCR). The outcome of interest was all-cause mortality. If no death information was available, cases were assumed to be alive through December 31, 1998.

Life table methods using six-month intervals were used to calculate crude survival rates for up to 10 years (Namboodiri and Suchindran 1987). SAS® PROC LIFETEST was used for these analyses (SAS Institute Inc. 1997). Although the crude survival rate is actually a proportion, in standard terminology it is referred to as a "rate". The relative survival rate is a measure of the influence of breast cancer on normal life expectancy, because it is obtained by adjusting the crude survival for the average life expectancy of the general population of the same age as women diagnosed with breast cancer. (A more detailed description can be found in the monograph on cancer survival in Ontario (McLaughlin *et al.* 1995).) Since it is generally acknowledged that cause of death information on death certificates is often not accurate enough to determine whether an individual died from his or her original cancer, the relative survival rate is the preferred method for reporting survival from cancer registry data. A FORTRAN program developed by Hakulinen et al. was used for the relative survival analyses (Hakulinen and Abewickrama 1985).

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Appendices

Appendix A. World and Canadian standard populations and Ontario 1996 population

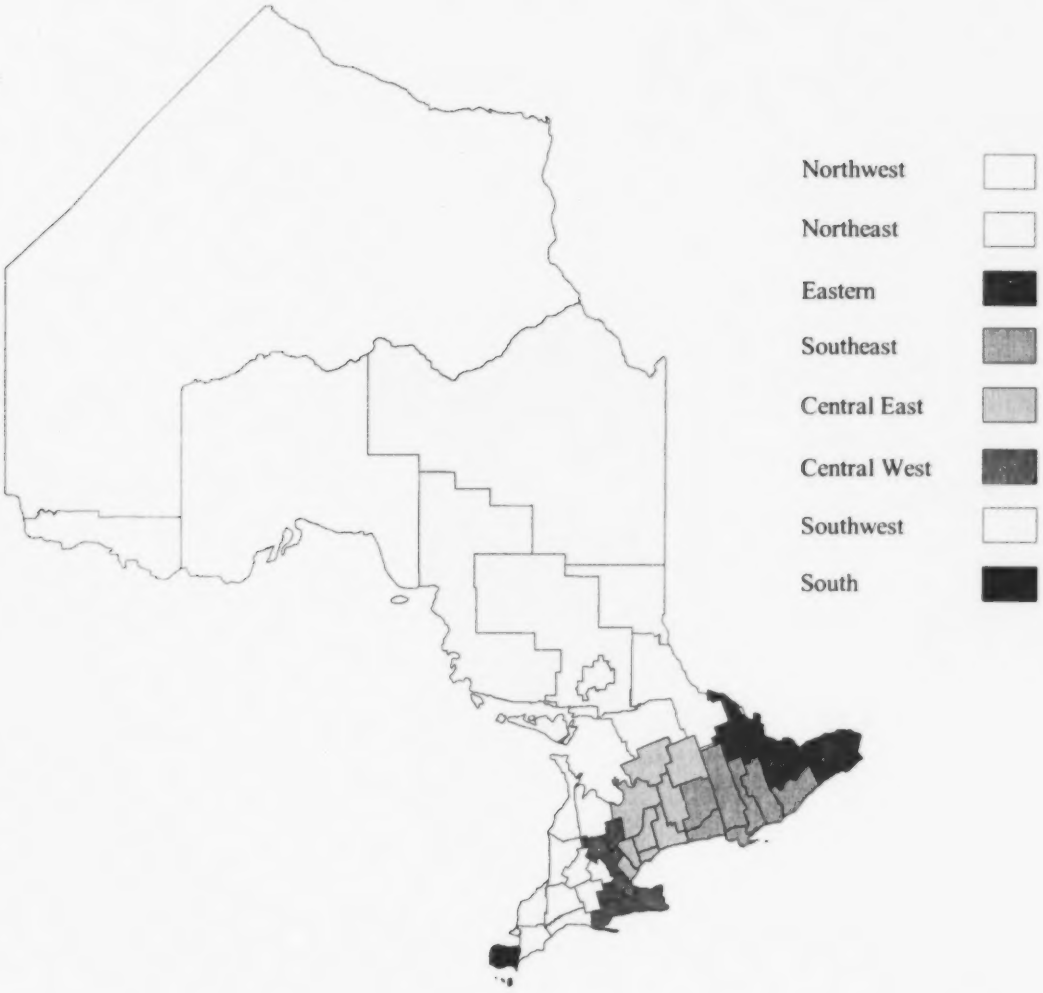
Age	World Standard Population[1]	Canadian 1991 Population[2]	Ontario 1996 Population[3]
0-4	12,000	6946.4	756,053
5-9	10,000	6945.4	760,338
10-14	9,000	6803.4	740,080
15-19	9,000	6849.5	721,396
20-24	8,000	7501.6	747,174
25-29	8,000	8994.4	826,426
30-34	6,000	9240.0	994,836
35-39	6,000	8338.8	973,241
40-44	6,000	7606.3	865,319
45-49	6,000	5953.6	790,268
50-54	5,000	4764.9	608,636
55-59	4,000	4404.1	501,217
60-64	4,000	4232.6	459,364
65-69	3,000	3857.0	431,223
70-74	2,000	2965.9	374,247
75-79	1,000	2212.7	255,754
80-84	500	1359.5	167,495
85+	500	1023.7	127,809
Total	**100,000**	**100,000**	**11,100,876**

[1] Parkin et al. 1997

[2] Statistics Canada 1994. Represented for convenience as the proportional distribution across age groups, rather than as actual population counts

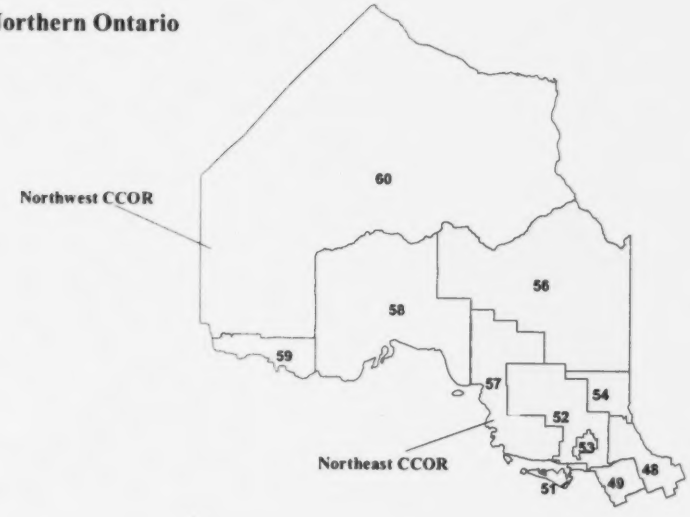
[3] Statistics Canada 1999

Appendix B. Cancer Care Ontario Regions (CCORs) showing census divisions



Appendix B (continued). Cancer Care Ontario Regions (CCORs) showing census divisions

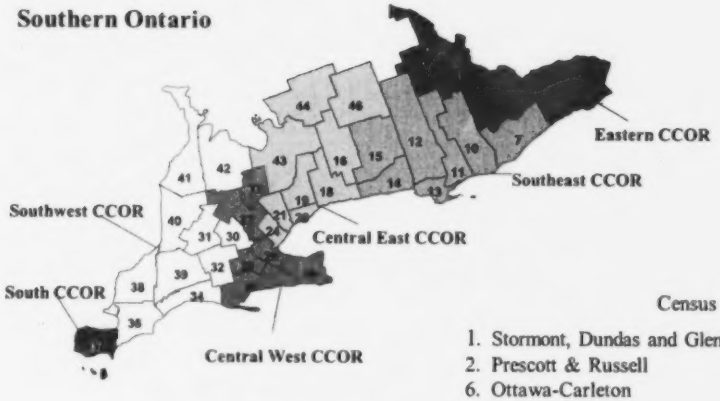
Northern Ontario



Census Divisions

48. Nipissing
49. Parry Sound
51. Manitoulin Island
52. Sudbury District
53. Sudbury R.M.
54. Timiskaming
56. Cochrane
57. Algoma
58. Thunder Bay
59. Rainy River
60. Kenora

Southern Ontario

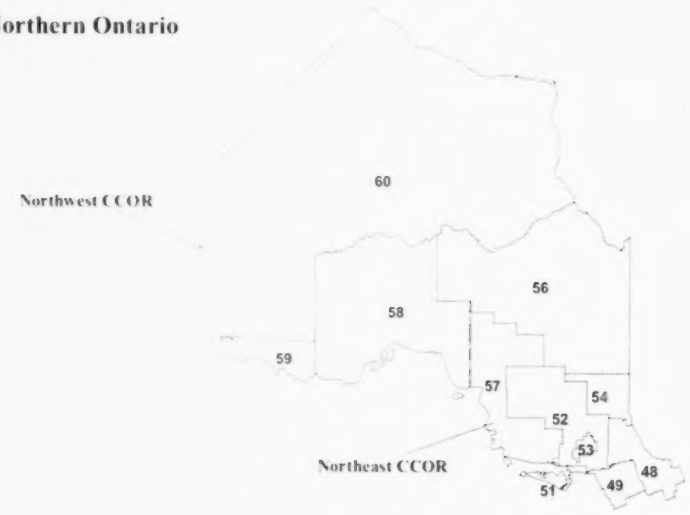


Census Divisions

1. Stormont, Dundas and Glengarry
2. Prescott & Russell
6. Ottawa-Carleton
7. Leeds & Grenville
9. Lanark
10. Frontenac
11. Lennox & Addington
12. Hastings
13. Prince Edward
14. Northumberland
15. Peterborough
16. Victoria
18. Durham
19. York
20. Toronto
21. Peel
22. Dufferin
23. Wellington
24. Halton
25. Hamilton-Wentworth
26. Niagara
28. Haldimand-Norfolk
29. Brant
30. Waterloo
31. Perth
32. Oxford
34. Elgin
36. Kent
37. Essex
38. Lambton
39. Middlesex
40. Huron
41. Bruce
42. Grey
43. Simcoe
44. Muskoka
46. Haliburton
47. Renfrew

Appendix B (continued). Cancer Care Ontario Regions (CCORs) showing census divisions

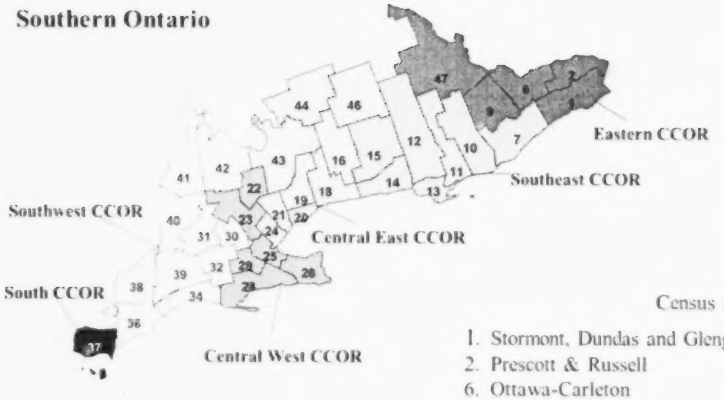
Northern Ontario



Census Divisions

48. Nipissing
49. Parry Sound
51. Manitoulin Island
52. Sudbury District
53. Sudbury R.M.
54. Timiskaming
56. Cochrane
57. Algoma
58. Thunder Bay
59. Rainy River
60. Kenora

Southern Ontario



Census Divisions

1. Stormont, Dundas and Glengarry
2. Prescott & Russell
6. Ottawa-Carleton
7. Leeds & Grenville
9. Lanark
10. Frontenac
11. Lennox & Addington
12. Hastings
13. Prince Edward
14. Northumberland
15. Peterborough
16. Victoria
18. Durham
19. York
20. Toronto
21. Peel
22. Dufferin
23. Wellington
24. Halton
25. Hamilton-Wentworth
26. Niagara
28. Haldimand-Norfolk
29. Brant
30. Waterloo
31. Perth
32. Oxford
34. Elgin
36. Kent
37. Essex
38. Lambton
39. Middlesex
40. Huron
41. Bruce
42. Grey
43. Simcoe
44. Muskoka
46. Haliburton
47. Renfrew

Appendix C.
Ontario Public Health Units (PHUs)

01. Algoma
02. Brant
03. Bruce-Grey-Owen Sound
04. Durham
05. Eastern Ontario
06. Elgin-St. Thomas
07. Windsor-Essex
08. Toronto
09. Haldimand-Norfolk
10. Haliburton-Kawartha-Pine Ridge
11. Halton
12. Hamilton-Wentworth
13. Hastings-Prince Edward
14. Huron
15. Kent-Chatham
16. Kingston-Frontenac-Lennox-Addington
17. Lambton
18. Leeds-Grenville-Lanark
19. Middlesex-London
20. Muskoka-Parry Sound
21. Niagara
22. North Bay and District
23. Northwestern
24. Ottawa-Carleton
25. Oxford
26. Peel
27. Perth
28. Peterborough
29. Porcupine
30. Renfrew
31. Simcoe
32. Sudbury and District
33. Thunder Bay
34. Timiskaming
35. Waterloo
36. Wellington-Dufferin-Guelph
37. York

Appendix C (continued). Ontario Public Health Units (PHUs) showing corresponding census divisions

Public Health Unit	Census divisions
Algoma	Algoma
Brant	Brant
Bruce-Grey-Owen Sound	Bruce
	Grey
Durham	Durham
Eastern Ontario	Prescott and Russell
	Stormont, Dundas and Glengarry
Elgin-St. Thomas	Elgin
Haldimand-Norfolk	Haldimand-Norfolk
Haliburton-Kawartha-Pine Ridge	Haliburton
	Northumberland
	Victoria
Halton	Halton
Hamilton-Wentworth	Hamilton-Wentworth
Hastings-Prince Edward	Hastings
	Prince Edward
Huron	Huron
Kent-Chatham	Kent
Kingston-Frontenac-Lennox-Addington	Frontenac
	Lennox and Addington
Lambton	Lambton
Leeds-Grenville-Lanark	Lanark
	Leeds and Grenville
Middlesex-London	Middlesex
Muskoka-Parry Sound	Muskoka
	Parry Sound
Niagara	Niagara
North Bay and District	Nipissing
Northwestern	Kenora
	Rainy River
Ottawa-Carleton	Ottawa-Carleton
Oxford	Oxford
Peel	Peel
Perth	Perth
Peterborough	Peterborough
Porcupine	Cochrane
Renfrew	Renfrew
Simcoe	Simcoe
Sudbury	Manitoulin Island
	Sudbury District
	Sudbury R.M.
Thunder Bay	Thunder Bay
Timiskaming	Timiskaming
Toronto	Toronto
Waterloo	Waterloo
Wellington-Dufferin-Guelph	Dufferin
	Wellington
Windsor-Essex	Essex
York	York

Appendix D. Description of morphologic subgroups for breast cancer

Subgroup[1]	ICDO-2 morphology code[2]
Carcinoma	8010-8573
Adenocarcinoma	8140-8573
Adenocarcinoma, NOS	8140
Infiltrating duct carcinoma	8500, 8521
Mucinous adenocarcinoma	8480, 8481
Comedocarcinoma	8501
Lobular carcinoma	8520
Infiltrating duct and lobular carcinoma	8522
Medullary carcinoma	8510, 8512
Paget's disease	8540-8543
Other specified adenocarcinoma	8141-8473, 8490, 8502, 8503, 8504, 8511, 8529, 8530, 8550-8573
Other specified carcinoma	8030-8120
Carcinoma, NOS	8010-8022
Sarcoma	8680-8713, 8800-8920, 8990-8991, 9040-9055, 9120-9134, 9140-9340, 9540-9581
Other specified types of malignant neoplasms	8720-8790, 8930-8933 8940, 8950-8982, 9000-9030, 9060-9110, 9350-9370, 9380-9512 9530-9539, 9673, 9715
Unspecified morphology	8000-8004, 9990

[1] Not all codes in each range apply to the breast

[2] ICDO-2 (International Classification of Diseases for Oncology, 2nd edition)